

STIC Search Report Biotech-Chem Library

STIC Database Tracking Number: 143640

TO: Tamthom Troung Location: REM-5C18

Art Unit: 1624

Monday, February 07, 2005

Case Serial Number: 10/075954

From: Noble Jarrell

Location: Biotech-Chem Library

Rem 1B71

Phone: 272-2556

Noble.jarrell@uspto.gov

Search Notes	a process		15/45		
		2			



```
=> d his
```

L1

(FILE 'HOME' ENTERED AT 11:20:28 ON 07 FEB 2005)

FILE 'HCAPLUS' ENTERED AT 11:20:35 ON 07 FEB 2005

1 US20020193377/PN

E US2001-268661/AP.PRN

L2 1 US2001-268661P/AP,PRN

L3 1 L1-2

FILE 'REGISTRY' ENTERED AT 11:21:44 ON 07 FEB 2005

FILE 'HCAPLUS' ENTERED AT 11:21:46 ON 07 FEB 2005

L4 TRA L3 1- RN : 441 TERMS

FILE 'REGISTRY' ENTERED AT 11:21:48 ON 07 FEB 2005 L5 441 SEA L4

FILE 'WPIX' ENTERED AT 11:21:54 ON 07 FEB 2005

L6 1 US20020193377/PN L7 1 US2001-268661P/AP.PRN E US2001-268661/AP.PRN

L8 1 L6-7

=> b hcap

FILE 'HCAPLUS' ENTERED AT 11:22:40 ON 07 FEB 2005 USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT. PLEASE SEE "HELP USAGETERMS" FOR DETAILS. COPYRIGHT (C) 2005 AMERICAN CHEMICAL SOCIETY (ACS)

Copyright of the articles to which records in this database refer is held by the publishers listed in the PUBLISHER (PB) field (available for records published or updated in Chemical Abstracts after December 26, 1996), unless otherwise indicated in the original publications. The CA Lexicon is the copyrighted intellectual property of the the American Chemical Society and is provided to assist you in searching databases on STN. Any dissemination, distribution, copying, or storing of this information, without the prior written consent of CAS, is strictly prohibited.

FILE COVERS 1907 - 7 Feb 2005 VOL 142 ISS 7 FILE LAST UPDATED: 6 Feb 2005 (20050206/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d. a11 13

- L3 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2005 ACS on STN
- AN 2002:637660 HCAPLUS
- DN 137:185501
- ED Entered STN: 23 Aug 2002
- TI Preparation of quinazolines as specific inhibitors of type-13 matrix metalloprotease
- IN Andrianjara, Charles; Chantel-Barvian, Nicole; Gaudilliere, Bernard; Jacobelli, Henri; Ortwine, Daniel Fred; Patt, William Chester; Pham, Ly; Kostlan, Catherine Rose; Wilson, Michael William
- PA Warner-Lambert Company, USA
- SO PCT Int. Appl., 264 pp. CODEN: PIXXD2
- DT Patent
- LA English

```
ICM C07D239-96
     ICS C07D401-12; C07D405-12; C07D409-12; C07D405-14; C07D409-14;
          C07D471-04: C07D403-12: C07D403-10: C07D410-10: C07D413-10:
          C07D401-06; A61K031-5025; A61K031-505
    28-16 (Heterocyclic Compounds (More Than One Hetero Atom))
     Section cross-reference(s): 1
FAN.CNT 1
     PATENT NO.
                        KIND DATE
                                          APPLICATION NO.
                                                                DATE
     -----
                        ----
                              -----
                                          -----
    WO 2002064572
                              20020822 WO 2002-EP1979
                                                                20020211 <--
PΤ
                        A1
        W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN.
            CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
           · GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
            LS. LT. LU. LV. MA. MD. MG. MK. MN. MW. MX. MZ. NO. NZ. OM. PH.
            PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
            UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU,
            TJ, TM
        RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH.
            CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR.
            BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
                        AA 20020822 CA 2002-2437122
     CA 2437122
                                                                20020211 <--
                            20031210
    EP 1368324
                                        EP 2002-722137
                                                                20020211 <--
                        A1
        R: AT. BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
            IE, SI, LT, LV, FI, RO, MK, CY, AL. TR
     EE 200300384
                              20031215
                                         EE 2003-384
                                                                20020211 <--
                        Α
     JP 2004523546
                              20040805
                                          JP 2002-564505
                                                                20020211 <--
                        T2
    US 2002193377
                              20021219
                                        US 2002-75954
                                                                20020213 <--
                         A1
    NO 2003003593
                         Α
                               20030813
                                         NO 2003-3593
                                                                20030813 <--
PRAI US 2001-268661P
                        р
                               20010214 <--
    WO 2002-EP1979
                         W
                              20020211
CLASS
                                                                          come man'y
 PATENT NO.
                CLASS PATENT FAMILY CLASSIFICATION CODES
 _____
               .....
 WO 2002064572
                ICM
                       C07D239-96
                       C07D401-12; C07D405-12; C07D409-12; C07D405-14;
                ICS
                       C07D409-14; C07D471-04; C07D403-12; C07D403-10;
                       C07D410-10; C07D413-10; C07D401-06; A61K031-5025;
                       A61K031-505
 JP 2004523546
                FTERM
                      4C063/AA01: 4C063/AA03: 4C063/BB03: 4C063/BB06:
                       4C063/BB08: 4C063/BB09: 4C063/CC31: 4C063/CC47:
                       4C063/CC58: 4C063/CC81: 4C063/CC92: 4C063/DD12:
                       4C063/DD28; 4C063/DD31; 4C063/EE01; 4C065/AA04;
                       4C065/AA05; 4C065/BB11; 4C065/CC01; 4C065/DD03;
                       4C065/EE02: 4C065/HH08: 4C065/JJ01: 4C065/KK01:
                       4C065/KK09; 4C065/LL04; 4C065/PP03; 4C065/PP07;
                       4C065/PP12; 4C065/QQ04; 4C065/QQ05; 4C086/AA01;
                       4C086/AA02; 4C086/AA03; 4C086/AA04; 4C086/BC46;
                       4C086/BC62; 4C086/BC71; 4C086/BC73; 4C086/CB09;
                       4C086/GA07; 4C086/GA08; 4C086/GA09; 4C086/GA12;
                       4C086/MA01; 4C086/MA02; 4C086/MA03; 4C086/MA04;
                       4C086/MA05; 4C086/NA14; 4C086/ZA15; 4C086/ZA33;
                       4C086/ZA36: 4C086/ZA45: 4C086/ZA67: 4C086/ZA68:
                       4C086/ZA96; 4C086/ZA97; 4C086/ZB15; 4C086/ZB26;
                       4C086/ZC20: 4C086/ZC41: 4C086/ZC52
0S
    CASREACT 137:185501; MARPAT 137:185501
GΙ
```

$$(R^2)_m - (Z^1)_n - Z + X^2 \times X^1 + X^3 + X^3 = X^3 + X^3$$

Title compds. I [R1 = H, amino, alkyl, alkenyl, alkynyl, alkylamino, aryl, heterocycle. etc.: W = 0, S, =N-R'; R' = alkyl, OH, CN; X1-3 = N, C-R6; R6= H, alkyl, amino, alkylamino, etc.; Y = O, S, NH, N-alkyl; Z = O, S, NR7; R7 = H, alkyl, aryl, aryl, heteroaryl, etc.; n = 1-8; Z1 = alkyl; A = (non)aromatic, 5- or 6-membered monocycle comprising from 0 to 4 heteroatoms selected from N. O. S. etc.; m = 0-7; R2 = alkyl, halo, CN, NO2, SCF3. CF3. OCF3. etc.; R3 = H, alkyl, alkenyl, alkynyl, etc.] were prepared Over 200 synthetic examples were provided. For instance, di-Me 4-aminoisophthalate was reacted with benzylisocyanate and heated to 95-100.degree. overnight to give Me 3-benzyl-2,4-dioxo-1,2,3,4tetrahydroquinazoline-6-carboxylate which was saponified (dioxaneaq, LiOH. reflux) to give the carboxylic acid. This intermediate was coupled with benzylamine to afford II. Selected examples of I had IC50 = 2.25 - 0.001.mu.M for MMP13 and IC50 > 100 .mu.M for MMP1, MMP2, MMP3, MMP7, MMP9, MMP12 and MMP14; II had IC50 = 0.193 .mu.M for MMP13. Compds. I are useful for the treatment of osteoarthritis and rheumatoid arthritis. quinazoline mmp matrix metalloprotease inhibitor prepn

IT Antiarteriosclerotics

(antiatherosclerotics; preparation of quinazolines as specific inhibitors of type- $13\ matrix\ metalloprotease$)

IT Lung, disease

IT Heart, disease

(failure: preparation of quinazolines as specific inhibitors of type-13 matrix metalloprotease)

IT Intestine, disease

(inflammatory: preparation of quinazolines as specific inhibitors of type-13 matrix metalloprotease) $\,$

IT Eye, disease

(macula, senile degeneration; preparation of quinazolines as specific inhibitors of type-13 matrix metalloprotease)

IT Antiarthritics

Antiasthmatics

Antirheumatic agents

Antitumor agents

Arthritis

Asthma

Atherosclerosis

Human

Multiple sclerosis

Neoplasm

Osteoarthritis

Osteoporosis

Periodontium, disease

Psoriasis

Rheumatoid arthritis

```
metalloprotease)
   Multiple sclerosis
    Osteoporosis
       (therapeutic agents: preparation of quinazolines as specific inhibitors of
       type-13 matrix metalloprotease)
  449208-02-0P, 3-Benzyl-2.4-dioxo-1,2,3,4-tetrahydroquinazoline-6-
    carboxylic acid (4-pyridylmethyl)amide 449208-14-4P 449208-50-8P.
    1-Methyl-2,4-dioxo-1,2,3,4-tetrahydroquinazoline-6-carboxylic acid
    [benzo[1,3]dioxol-5-ylmethyl]amide 449208-52-0P, Methyl
    4-[[6-(4-methoxybenzylcarbamoyl)-1-methyl-2.4-dioxo-1.4-dihydro-2H-
    quinazolin-3-yl]methyl]benzoate 449208-55-3P, 4-[[6-(4-
    Methoxybenzylcarbamoyl)-1-methyl-2.4-dioxo-1.4-dihydro-2H-quinazolin-3-
    yl]methyl]benzoic acid 449208-57-5P. 3-Benzyl-2.4-dioxo-1.2.3.4-
    tetrahydroquinazoline-6-carboxylic acid benzyl ester 449208-82-6P
    449209-00-1P. [4-[[6-(4-Methoxybenzylcarbamoyl)-1-methyl-2,4-dioxo-1.4-
    dihydro-2H-quinazolin-3-yl]methyl]phenyl]acetic acid 449209-16-9P,
    Methyl 3-[[6-(4-methoxybenzylcarbamoyl)-1-methyl-2,4-dioxo-1,4-dihydro-2H-
    quinazolin-3-yl]methyl]benzoate 449209-18-1P, (E)-Methyl
    4-[6-(4-methoxybenzylcarbamoyl)-1-methyl-2.4-dioxo-1.4-dihydro-2H-
    quinazolin-3-yl]but-2-enoate 449209-20-5P, Methyl 5-[[6-(4-
    methoxybenzylcarbamoyl)-1-methyl-2,4-dioxo-1,4-dihydro-2H-quinazolin-3-
    yl]methyl]furan-2-carboxylate 449209-22-7P, Methyl 5-[[6-(4-
    methoxybenzylcarbamoyl)-1-methyl-2,4-dioxo-1,4-dihydro-2H-quinazolin-3-
    yl]methyl]thiophene-2-carboxylate 449209-24-9P 449209-37-4P. Methyl
    2-chloro-4-[[6-(4-methoxybenzylcarbamoyl)-1-methyl-2,4-dioxo-1,4-dihydro-
    2H-quinazolin-3-yl]methyl]benzoate 449209-43-2P, Methyl
    2-methoxy-4-[[6-(4-methoxybenzylcarbamoyl)-1-methyl-2.4-dioxo-1.4-dihydro-
    2H-quinazolin-3-yl]methyl]benzoate 449209-44-3P, 2-Methoxy-4-[[6-(4-
    methoxybenzylcarbamoyl)-1-methyl-2,4-dioxo-1,4-dihydro-2H-quinazolin-3-
    yl]methyl]benzoic acid 449209-45-4P, Methyl 2-hydroxy-4-[[6-(4-
    methoxybenzylcarbamoyl)-1-methyl-2,4-dioxo-1,4-dihydro-2H-quinazolin-3-
    yl]methyl]benzoate 449209-47-6P, Methyl 2-methyl-4-[[6-(4-
    methoxybenzylcarbamoyl)-1-methyl-2,4-dioxo-1,4-dihydro-2H-quinazolin-3-
    yl]methyl]benzoate 449209-49-8P 449209-52-3P
                                                     449209-54-5P. Methyl
    4-[[6-(3-methoxybenzylcarbamoyl)-1-methyl-2,4-dioxo-1,4-dihydro-2H-
    quinazolin-3-yl]methyl]benzoate 449209-60-3P. 4-[[1-Methyl-6-((4-
    (methylsulfanyl)benzyl)carbamoyl)-2,4-dioxo-1,4-dihydro-2H-quinazolin-3-
    yl]methyl]benzoic acid methyl ester 449209-70-5P, 3-(4-Methoxybenzyl)-1-
    methy1-2,4-dioxo-1,2,3,4-tetrahydroquinazoline-6-carboxylic acid
    ((pyridin-4-yl)methyl)amide 449209-75-0P, Methyl 4-[[1-methyl-2,4-dioxo-
    6-[(pyridin-4-ylmethyl)carbamoyl]-1,4-dihydro-2H-quinazolin-3-
    yl]methyl]benzoate 449209-89-6P 449209-90-9P
                                                      449209-91-0P
    449209-95-4P 449209-98-7P. [5-[[6-(4-(Methoxy)benzylcarbamoyl)-1-methyl-
    2.4-dioxo-1.4-dihydro-2H-quinazolin-3-yl]methyl]pyridin-2-yl]carbamic acid
    tert-butyl ester 449210-36-0P, 4'-[[6-((4-Methoxybenzyl)carbamoyl)-1-
    methyl-2.4-dioxo-1.4-dihydro-2H-quinazolin-3-yl]methyl]biphenyl-2-
    carboxylic acid methyl ester 449210-88-2P, tert-Butyl
    1-[4-[[6-(4-methoxybenzylcarbamoyl)-1-methyl-2,4-dioxo-1,4-dihydro-2H-
    quinazolin-3-yl]methyl]phenyl]cyclopropanecarboxylate 449210-90-6P.
    3-Benzyl-6-benzylsulfanyl-1-methyl-1H-quinazoline-2.4-dione
    449210-98-4P. 4-[[6-(4-Methoxybenzylcarbamoyl)-1-methyl-2,4-dioxo-1.4-
    dihydro-2H-quinazoline-3-yl]methyl]benzoic acid chloromethyl ester
    449210-99-5P 449211-01-2P 474663-15-5P, Ethyl 2-Fluoro-4-[[6-(4-
    methoxybenzylcarbamoyl)-1-methyl-2.4-dioxo-1.4-dihydro-2H-quinazolin-3-
    yl]methyl]benzoate
    RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic
    preparation); THU (Therapeutic use); BIOL (Biological study); PREP
    (Preparation); RACT (Reactant or reagent); USES (Uses)
       (MMP13 inhibitor; preparation of quinazolines as specific inhibitors of
       type-13 matrix metalloprotease)
IT 449208-01-9P, 3-Benzyl-2,4-dioxo-1,2,3,4-tetrahydroquinazoline-6-
    carboxylic acid benzylamide 449208-03-1P. 3-Benzyl-2.4-dioxo-1.2.3.4-
    tetrahydroquinazoline-6-carboxylic acid (benzo[1.3]dioxol-5-ylmethyl)amide
```

(preparation of quinazolines as specific inhibitors of type-13 matrix

449208-04-2P. 3-Benzyl-2.4-dioxo-1.2.3.4-tetrahydroquinazoline-6carboxylic acid (2-thienylmethyl)amide 449208-06-4P. 3-Benzyl-2,4-dioxo-1,2,3,4-tetrahydroguinazoline-6-carboxylic acid (3-pyridylmethyl)amide 449208-07-5P 449208-08-6P 449208-09-7P 449208-10-0P. 3-Benzyl-1-methyl-2.4-dioxo-1.2.3.4-tetrahydroquinazoline-6carboxylic acid (benzo[1,3]dioxol-5-ylmethyl)amide 449208-11-1P. 3-Benzyl-1-methyl-2.4-dioxo-1.2.3.4-tetrahydroquinazoline-6-carboxylic acid benzylamide 449208-12-2P, Methyl 4-[[[1-(3-benzyl-1-methyl-2.4dioxo-1,2,3,4-tetrahydroquinazolin-6-yl)methanoyl]amino]methyl]benzoate 449208-13-3P, 3-Benzyl-1-methyl-2,4-dioxo-1,2,3,4-tetrahydroquinazoline-6carboxylic acid [4-hydroxy-3-methoxybenzyl]amide 449208-15-5P. 3-Benzyl-1-methyl-2.4-dioxo-1,2,3.4-tetrahydroquinazoline-6-carboxylic acid (4-pyridylmethyl)amide 449208-16-6P. 1-Methyl-2.4-dioxo-3-phenethyl-1,2,3,4-tetrahydroguinazoline-6-carboxylic acid [benzo[1,3]dioxol-5ylmethyl]amide 449208-20-2P, 3-(4-Methoxybenzyl)-2.4-dioxo-1.2.3.4tetrahydroquinazoline-6-carboxylic acid [benzo[1,3]dioxol-5-ylmethyl]amide 449208-22-4P. 3-(4-Methoxybenzyl)-1-methyl-2.4-dioxo-1.2.3.4tetrahydroquinazoline-6-carboxylic acid [benzo[1.3]dioxol-5-ylmethyl]amide 449208-23-5P 449208-25-7P, 3-(1-(Naphth-1-yl)ethyl)-2.4-dioxo-1.2.3.4tetrahydroquinazoline-6-carboxylic acid [benzo[1,3]dioxol-5-ylmethyl]amide 449208-26-8P. 2.4-Dioxo-3-((pyridin-4-yl)methyl)-1.2.3.4tetrahydroquinazoline-6-carboxylic acid [benzo[1.3]dioxol-5-ylmethyl]amide 449208-32-6P. 2.4-Dioxo-3-(thien-2-ylmethyl)-1.2.3.4-tetrahydroquinazoline-6-carboxylic acid benzylamide 449208-36-0P, 1-Methyl-2.4-dioxo-3-(thien-2-ylmethyl)-1.2.3.4-tetrahydroquinazoline-6-carboxylic acid benzylamide 449208-37-1P, 2.4-Dioxo-3-(thien-2-ylmethyl)-1.2.3.4-tetrahydroquinazoline-6-carboxylic acid [benzo[1,3]dioxol-5-ylmethyl]amide 449208-38-2P. 1-Methyl-2.4-dioxo-3-(thien-2-ylmethyl)-1.2,3.4-tetrahydroquinazoline-6carboxylic acid [benzo[1.3]dioxol-5-ylmethyl]amide 449208-39-3P. 3-(4-Chlorobenzyl)-2,4-dioxo-1,2,3,4-tetrahydroquinazoline-6-carboxylic acid [benzo[1,3]dioxol-5-ylmethyl]amide 449208-40-6P. 3-(4-Chlorobenzyl)-1-methyl-2,4-dioxo-1,2,3,4-tetrahydroquinazoline-6carboxylic acid [benzo[1,3]dioxol-5-ylmethyl]amide 449208-41-7P. 1.3-Dimethyl-2.4-dioxo-1.2.3.4-tetrahydroguinazoline-6-carboxylic acid [benzo[1.3]dioxol-5-ylmethyl]amide 449208-42-8P. 3-((Benzo[1.3]dioxol-5yl)methyl)-2,4-dioxo-1,2,3,4-tetrahydroquinazoline-6-carboxylic acid [benzo[1,3]dioxol-5-ylmethyl]amide 449208-46-2P, 3-((Benzo[1,3]dioxol-5yl)methyl)-1-methyl-2.4-dioxo-1.2.3.4-tetrahydroquinazoline-6-carboxylic acid [benzo[1,3]dioxol-5-ylmethyl]amide 449208-47-3P. 3-Benzyl-1-ethyl-2,4-dioxo-1,2,3,4-tetrahydroquinazoline-6-carboxylic acid [benzo[1,3]dioxol-5-ylmethyl]amide 449208-48-4P, 3-Benzyl-1cyclopropylmethyl-2,4-dioxo-1,2,3,4-tetrahydroquinazoline-6-carboxylic acid [benzo[1.3]dioxol-5-ylmethyl]amide 449208-49-5P. 3-Benzyl-1-isobutyl-2.4-dioxo-1.2.3.4-tetrahydroquinazoline-6-carboxylic acid [benzo[1,3]dioxol-5-ylmethyl]amide 449208-56-4P. 1-Methyl-2,4-dioxo-3-((E)-3-phenylpropenyl)-1,2,3,4-tetrahydroquinazoline-6-carboxylic acid [benzo[1,3]dioxol-5-ylmethyl]amide 449208-58-6P. 3-Benzyl-1-methyl-2.4-dioxo-1.2.3.4-tetrahydroquinazoline-6-carboxylic acid benzyl ester 449208-59-7P, 3-Benzyl-2,4-dioxo-1,2,3,4tetrahydroquinazoline-6-carboxylic acid 4-pyridylmethyl ester 449208-61-1P. 3-Benzy1-2.4-dioxo-1.2.3.4-449208-60-0P tetrahydroquinazoline-6-carboxylic acid [Benzo[1.3]dioxol-5-yl]methyl 449208-62-2P, 3-Benzyl-1-methyl-2.4-dioxo-1.2.3.4tetrahydroquinazoline-6-carboxylic acid [Benzo[1,3]dioxol-5-yl]methyl 449208-63-3P, 1-Benzyl-2.4-dioxo-3-((pyridin-4-yl)methyl)-1.2.3.4tetrahydroquinazoline-6-carboxylic acid benzyl ester 449208-64-4P. 2.4-Dioxo-3-(thien-2-ylmethyl)-1.2.3.4-tetrahydroquinazoline-6-carboxylic acid 4-Pyridylmethyl ester 449208-65-5P. 3-((Benzo[1,3]dioxol-5yl)methyl)-2.4-dioxo-1.2.3.4-tetrahydroquinazoline-6-carboxylic acid 4-Pyridylmethyl ester 449208-66-6P, Benzyl 3-benzyl-2.4-dioxo-1.2.3.4tetrahydropyrido[2,3-d]pyrimidine-6-carboxylate 449208-67-7P. 3-Benzyl-6-methyl-1H-pyrido[2,3-d]pyrimidine-2,4-dione 449208-69-9P. 4-Pyridylmethyl 3-benzyl-2.4-dioxo-1.2.3.4-tetrahydropyrido[2.3d]pyrimidine-6-carboxylate 449208-70-2P. 3-Benzyl-4-oxo-2-thioxo-1.2.3.4-

```
tetrahydroquinazoline-6-carboxylic acid [benzo[1,3]dioxol-5-ylmethyl]amide
449208-71-3P, 4-[[6-(4-Hydroxybenzylcarbamoyl)-1-methyl-2,4-dioxo-1,4-
dihydro-2H-guinazolin-3-yl]methyl]benzoic acid
                                               449208-72-4P
                                                          449208-77-9P
449208-73-5P
              449208-74-6P
                             449208-75-7P
                                           449208-76-8P
449208-78-0P
              449208-79-1P
                             449208-80-4P
                                            449208-81-5P
                                                           449208-83-7P
449208-84-8P
                             449208-87-1P
                                            449208-88-2P
                                                           449208-89-3P
              449208-85-9P
                             449208-92-8P
449208-90-6P
              449208-91-7P
                                           449208-93-9P, Ethyl
[6-(4-methoxybenzylcarbamoyl)-1-methyl-2.4-dioxo-1.4-dihydro-2H-quinazolin-
3-y1]acetate 449208-94-0P 449208-95-1P, Methyl 3-[6-(4-
methoxybenzylcarbamoyl)-1-methyl-2,4-dioxo-1,4-dihydro-2H-quinazolin-3-
yl]propionate 449208-96-2P, 3-[6-(4-Methoxybenzylcarbamoyl)-1-methyl-2.4-
dioxo-1,4-dihydro-2H-quinazolin-3-yl]propionic acid 449208-97-3P
449208-98-4P, 4-[6-(4-Methoxybenzylcarbamoyl)-1-methyl-2.4-dioxo-1.4-
dihydro-2H-guinazolin-3-yl]butyric acid 449208-99-5P, Methyl
[4-[[6-(4-methoxybenzylcarbamoyl)-1-methyl-2,4-dioxo-1,4-dihydro-2H-
quinazolin-3-yl]methyl]phenyl]acetate 449209-01-2P 449209-02-3P
              449209-06-7P 449209-07-8P 449209-09-0P
449209-04-5P
              449209-17-0P, 3-[[6-(4-Methoxybenzylcarbamoyl)-1-methyl-2.4-
449209-14-7P
dioxo-1,4-dihydro-2H-quinazolin-3-yl]methyl]benzoic acid 449209-19-2P.
4-[6-(4-Methoxybenzylcarbamoyl)-1-methyl-2.4-dioxo-1.4-dihydro-2H-
quinazolin-3-yl]but-2-enoic acid 449209-21-6P. 5-[[6-(4-
Methoxybenzylcarbamoyl)-1-methyl-2,4-dioxo-1,4-dihydro-2H-quinazolin-3-
yl]methyl]furan-2-carboxylic acid 449209-23-8P, 5-[[6-(4-
Methoxybenzylcarbamoyl)-1-methyl-2,4-dioxo-1,4-dihydro-2H-quinazolin-3-
yl]methyl]thiophene-2-carboxylic acid 449209-25-0P 449209-26-1P
              449209-28-3P
                            449209-29-4P
                                           449209-30-7P
                                                           449209-31-8P
449209-27-2P
                                            449209-36-3P
449209-32-9P
              449209-33-0P
                             449209-34-1P
                                                           449209-39-6P.
2-Chloro-4-[[6-(4-methoxybenzylcarbamoyl)-1-methyl-2,4-dioxo-1,4-dihydro-
2H-quinazolin-3-yl]methyl]benzoic acid 449209-40-9P
                                                      449209-41-0P
449209-46-5P. 2-Hydroxy-4-[[6-(4-methoxybenzylcarbamoyl)-1-methyl-2.4-
dioxo-1,4-dihydro-2H-quinazolin-3-yl]methyl]benzoic acid 449209-48-7P.
2-Methyl-4-[[6-(4-methoxybenzylcarbamoyl)-1-methyl-2.4-dioxo-1.4-dihydro-
2H-quinazolin-3-yl]methyl]benzoic acid 449209-53-4P 449209-59-0P.
4-[[6-(3-Methoxybenzylcarbamoyl)-1-methyl-2,4-dioxo-1,4-dihydro-2H-
quinazolin-3-yl]methyl]benzoic acid 449209-61-4P, 4-[[1-Methyl-6-(4-
methylsulfanylbenzylcarbamoyl)-2,4-dioxo-1,4-dihydro-2H-quinazolin-3-
yl]methyl]benzoic acid 449209-62-5P, 4-[[1-Methyl-2,4-dioxo-6-(4-
(trifluoromethoxy)benzylcarbamoyl)-1.4-dihydro-2H-quinazolin-3-
yl]methyl]benzoic acid methyl ester 449209-63-6P, Methyl
4-[[6-(4-fluorobenzylcarbamoyl)-1-methyl-2,4-dioxo-1,4-dihydro-2H-
quinazolin-3-yl]methyl]benzoate 449209-64-7P. 4-[[6-(4-
Fluorobenzylcarbamoyl)-1-methyl-2,4-dioxo-1,4-dihydro-2H-quinazolin-3-
yl]methyl]benzoic acid 449209-65-8P, Methyl 4-[[6-[(benzofurazan-5-
ylmethyl)carbamoyl]-1-methyl-2,4-dioxo-1,4-dihydro-2H-quinazolin-3-
yl]methyl]benzoate 449209-66-9P. 4-[[6-[(Benzofurazan-5-
ylmethyl)carbamoyl]-1-methyl-2,4-dioxo-1,4-dihydro-2H-quinazolin-3-
yl]methyl]benzoic acid 449209-67-0P, Methyl 4-[[6-(4-
methoxybenzylcarbamoyl)-2,4-dioxo-1,4-dihydro-2H-quinazolin-3-
yl]methyl]benzoate 449209-68-1P, Methyl 4-[[1-ethyl-6-(4-
methoxybenzylcarbamoyl)-2,4-dioxo-1,4-dihydro-2H-quinazolin-3-
y1]methy1]benzoate 449209-69-2P, 4-[[1-Ethy1-6-(4-
methoxybenzylcarbamoyl)-2,4-dioxo-1,4-dihydro-2H-quinazolin-3-
yl]methyl]benzoic acid 449209-71-6P, 3-(4-Hydroxybenzyl)-1-methyl-2.4-
dioxo-1,2,3,4-tetrahydroquinazoline-6-carboxylic acid ((pyridin-4-
yl)methyl)amide 449209-72-7P, 3-(4-Cyanobenzyl)-1-methyl-2.4-dioxo-
1.2.3.4-tetrahydroquinazoline-6-carboxylic acid ((pyridin-4-
y1)methy1)amide 449209-74-9P, 1-Methy1-2,4-dioxo-3-(3-(pyridin-4-
yl)propenyl)-1,2,3,4-tetrahydroquinazoline-6-carboxylic acid
((pyridin-4-y1)methy1)amide 449209-76-1P, 4-[[1-Methy1-2,4-dioxo-6-
[(pyridin-4-ylmethyl)carbamoyl]-1,4-dihydro-2H-quinazolin-3-
yl]methyl]benzoic acid hydrochloride 449209-77-2P, Methyl
[4-[[1-methy]-2.4-dioxo-6-[(pyridin-4-y]methy])carbamoy]]-1.4-dihydro-2H-
quinazolin-3-yl]methyl]phenyl]acetate 449209-78-3P, [4-[[1-Methyl-2.4-
dioxo-6-[(pyridin-4-ylmethyl)carbamoyl]-1.4-dihydro-2H-quinazolin-3-
```

yl]methyl]phenyl]acetic acid hydrochloride 449209-79-4P 449209-80-7P 449209-81-8P, Methyl [6-[(1,3-Benzodioxol-5-ylmethyl)carbamoyl]-3-benzyl-2,4-dioxo-1.4-dihydro-2H-quinazolin-1-yl]acetate 449209-82-9P. [6-[(1,3-Benzodioxol-5-ylmethyl)carbamoyl]-3-benzyl-2,4-dioxo-3,4-dihydro-2H-quinazolin-1-yl]acetic acid 449209-83-0P, Methyl 4-[[6-[(1.3benzodioxol-5-ylmethyl)carbamoyl]-1-methyl-2.4-dioxo-1.4-dihydro-2Hquinazolin-3-yl]methyl]benzoate 449209-84-1P, 4-[[6-[(1.3-Benzodioxol-5-ylmethyl)carbamoyl]-1-methyl-2.4-dioxo-1.4-dihydro-2H-quinazolin-3yl]methyl]benzoic acid 449209-85-2P, 3-Benzyl-1-methyl-2,4-dioxo-1,2,3.4tetrahydroquinazoline-6-carboxylic acid (4-(sulfamoyl)benzyl)amide 449209-86-3P, 3-Benzyl-1-methyl-2,4-dioxo-1,2,3,4-tetrahydroquinazoline-6carboxylic acid [3-(pyridin-4-ylsulfanyl)propyl]amide 449209-87-4P. 3-Benzyl-1-methyl-2,4-dioxo-1,2,3,4-tetrahydroquinazoline-6-carboxylic acid (4-morpholin-4-ylbutyl)amide 449209-88-5P 449209-92-1P. 3-Benzyl-1-methyl-2,4-dioxo-1,2,3,4-tetrahydroquinazoline-6-carboxylic acid (4-((dimethylcarbamoyl)methoxy)benzyl)amide 449209-93-2P 449209-96-5P, 3-Benzyl-1-methyl-2,4-dioxo-1,2,3,4-449209-94-3P tetrahydroquinazoline-6-carboxylic acid (4-(dimethylcarbamoyl)benzyl)amide 449209-97-6P 449209-99-8P 449210-00-8P, 1,3-Dimethyl-2,4-dioxo-1,2,3,4tetrahydropyrido[2,3-d]pyrimidine-6-carboxylic acid [benzo[1,3]dioxol-5ylmethyl]amide 449210-01-9P, 1.3-Dimethyl-2.4-dioxo-1.2.3.4tetrahydropyrido[3.4-d]pyrimidine-6-carboxylic acid [benzo[1.3]dioxol-5ylmethyl]amide 449210-03-1P, 3-Benzyl-1-methyl-2.4-dioxo-1.2.3.4tetrahydropyrido[2,3-d]pyrimidine-6-carboxylic acid [benzo[1,3]dioxol-5ylmethyl]amide 449210-07-5P, 4-[[6-(4-Methoxybenzylcarbamoyl)-1-methyl-2,4-dioxo-1,4-dihydro-2H-pyrido[2,3-d]pyrimidin-3-yl]methyl]benzoic acid 449210-11-1P 449210-12-2P 449210-13-3P, 3-Benzyl-1-methyl-2,4-dioxo-1,2,3,4-tetrahydropyrido[3,4-d]pyrimidine-6-carboxylic acid [benzo[1,3]dioxol-5-ylmethyl]amide 449210-20-2P, Methyl 4-[[6-(4-Methoxybenzylcarbamoyl)-1-methyl-2,4-dioxo-1,4-dihydro-2Hpyrido[3,4-d]pyrimidin-3-yl]methyl]benzoate 449210-23-5P. tert-Butyl 4-[[6-(4-methoxybenzylcarbamoyl)-1-methyl-2,4-dioxo-1,4-dihydro-2Hpyrido[3,4-d]pyrimidin-3-yl]methyl]benzoate 449210-24-6P. 4-[[6-(3-Methoxybenzylcarbamoyl)-1-methyl-2,4-dioxo-1,4-dihydro-2Hpyrido[3,4-d]pyrimidin-3-yl]methyl]benzoic acid 449210-27-9P 449210-28-0P, 3-Benzyl-1-methyl-6-(3-phenylpropionyl)-1H-quinazoline-2.4-449210-29-1P 449210-30-4P 449210-31-5P, 3-Benzyl-1-methyl-6-[2-(pyridin-4-ylsulfanyl)acetyl]-1H-quinazoline-2,4-dione 449210-32-6P 449210-33-7P 449210-34-8P 449210-37-1P, 4'-[[6-(4-Methoxybenzylcarbamoyl)-1-methyl-2.4-dioxo-1.4-dihydro-2H-quinazolin-3yl]methyl]biphenyl-2-carboxylic acid 449210-39-3P, 2-Fluoro-4-[[6-(4methoxybenzylcarbamoyl)-1-methyl-2,4-dioxo-1,4-dihydro-2H-quinazolin-3yl]methyl]benzoic acid 449210-40-6P. 2-Methoxy-4-[[6-(4methoxybenzylcarbamoyl)-1-methyl-2,4-dioxo-1,4-dihydro-2H-quinazolin-3yl]methyl]benzoic acid 2-dimethylaminoethyl ester 449210-41-7P. 4=[[6-(4-Methoxybenzylcarbamoyl)-1-methyl-2,4-dioxo-1,4-dihydro-2Hquinazolin-3-yl]methyl]-2-methylbenzoic acid 2-dimethylaminoethyl ester 449210-42-8P 449210-43-9P, [4-[6-(4-Methoxybenzylcarbamoyl)-1-methyl-2,4dioxo-1,4-dihydro-2H-quinazolin-3-yl]phenyl]acetic acid 449210-45-1P, 1-Methyl-3-(1-(naphthalen-1-yl)ethyl)-2,4-dioxo-1,2,3,4tetrahydroquinazoline-6-carboxylic acid [benzo[1,3]dioxol-5-ylmethyl]amide 449210-47-3P. 4-[[6-(4-Methoxybenzylcarbamoyl)-1-methyl-2,4-dioxo-1,4dihydro-2H-pyrido[3.4-d]pyrimidin-3-yl]methyl]benzoic acid 449210-49-5P. 3-(3-Fluorobenzyl)-1-methyl-2.4-dioxo-1,2,3,4-tetrahydroguinazoline-6carboxylic acid ((pyridin-4-yl)methyl)amide 449210-51-9P. 3-(3-Fluorobenzyl)-1-methyl-2,4-dioxo-1,2,3,4-tetrahydroquinazoline-6carboxylic acid ((2-methoxypyridin-4-yl)methyl)amide 449210-52-0P. 3-(3-Fluorobenzyl)-1-methyl-2,4-dioxo-1,2,3,4-tetrahydroquinazoline-6carboxylic acid ((pyridin-3-yl)methyl)amide 449210-53-1P 449210-55-3P, 1-Ethyl-3-(3-fluorobenzyl)-2,4-dioxo-1,2,3,4tetrahydroquinazoline-6-carboxylic acid ((pyridin-4-yl)methyl)amide 449210-56-4P, 1-Ethyl-3-(3-fluorobenzyl)-2.4-dioxo-1,2,3,4tetrahydroquinazoline-6-carboxylic acid ((pyridin-3-yl)methyl)amide 449210-57-5P 449210-61-1P, 3-(4-Bromobenzyl)-1-methyl-2.4-dioxo-1.2.3.4-

```
tetrahydroquinazoline-6-carboxylic acid ((2-methoxypyridin-4-
yl)methyl)amide 449210-62-2P, 3-(3,4-Difluorobenzyl)-1-methyl-2,4-dioxo-
1.2.3.4-tetrahydroguinazoline-6-carboxylic acid (pyridin-3-ylmethyl)amide
449210-66-6P. 3-(3.4-Difluorobenzyl)-1-methyl-2,4-dioxo-1,2,3,4-
tetrahydroquinazoline-6-carboxylic acid (pyridin-4-ylmethyl)amide
449210-67-7P 449210-68-8P, 3-(3-Chloro-4-fluorobenzyl)-1-methyl-2.4-
dioxo-1,2,3,4-tetrahydroquinazoline-6-carboxylic acid ((pyridin-4-
yl)methyl)amide 449210-72-4P 449210-73-5P 449210-74-6P
449210-75-7P 449210-76-8P. 3-(4-Chlorobenzyl)-1-methyl-2.4-dioxo-1.2.3.4-
tetrahydroquinazoline-6-carboxylic acid ((pyridin-4-yl)methyl)amide
449210-78-0P. 3-(4-Fluorobenzyl)-1-methyl-2,4-dioxo-1,2,3,4-
tetrahydroquinazoline-6-carboxylic acid ((pyridin-4-yl)methyl)amide
449210-79-1P. 3-(4-Fluorobenzyl)-1-methyl-2,4-dioxo-1,2,3,4-
tetrahydroquinazoline-6-carboxylic acid ((pyridin-3-yl)methyl)amide
449210-81-5P. 3-(4-Chlorobenzyl)-1-methyl-2,4-dioxo-1,2,3,4-
tetrahydroquinazoline-6-carboxylic acid ((pyridin-3-yl)methyl)amide
449210-82-6P 449210-84-8P 449210-85-9P, 3-(4-Fluorobenzyl)-1-methyl-
2.4-dioxo-1.2.3.4-tetrahydroquinazoline-6-carboxylic acid
((2-methoxypyridin-4-yl)methyl)amide 449210-87-1P, 3-(4-Chlorobenzyl)-1-
methyl-2,4-dioxo-1,2,3,4-tetrahydroquinazoline-6-carboxylic acid
((2-methoxypyridin-4-yl)methyl)amide 449210-89-3P, 1-[4-[[6-(4-
Methoxybenzylcarbamoyl)-1-methyl-2.4-dioxo-1.4-dihydro-2H-quinazolin-3-
yl]methyl]phenyl]cyclopropanecarboxylic acid 449210-92-8P.
3-Benzyl-1-methyl-6-((phenylmethyl)sulfinyl)-1H-quinazoline-2,4-dione
449210-93-9P, 3-Benzyl-1-methyl-6-((phenylmethyl)sulfonyl)-1H-quinazoline-
2.4-dione 449210-94-0P 449210-95-1P. 4-[[6-(4-Methoxybenzylcarbamoyl)-
1-methyl-2.4-dioxo-1.4-dihydro-2H-quinazoline-3-yl]methyl]benzoic acid
3-(dimethylamino)-2,2-dimethylpropyl ester 449210-96-2P.
4-[[6-((4-Methoxybenzyl)carbamoyl)-1-methyl-2.4-dioxo-1.4-dihydro-2H-
guinazoline-3-yl]methyl]benzoic acid 2-(dimethylamino)-2-methylpropyl
      449210-97-3P, 4-[[6-(4-Methoxybenzylcarbamoyl)-1-methyl-2.4-dioxo-
1,4-dihydro-2H-quinazoline-3-yl]methyl]benzoic acid 2-dimethylaminoethyl
        449211-00-1P 449211-04-5P 449211-08-9P 449211-12-5P.
4-[[6-((3-Methoxybenzy]carbamov])methy])-2.4-dioxo-1.4-dihydro-2H-
guinazolin-3-yl]methyl]benzoic acid methyl ester 449211-14-7P.
4-[[1-Ethyl-2.4-dioxo-6-((4-(trifluoromethoxy)benzyl)carbamoyl)-1.4-
dihydro-2H-quinazolin-3-yl]methyl]benzoic acid methyl ester
449211-16-9P. 4-[[1-Methy]-2,4-dioxo-6-[(pyridin-4-ylmethyl)carbamoyl]-1,4-
dihydro-2H-quinazolin-3-yl]methyl]benzoic acid 449211-18-1P.
[4-[[1-Methy]-2.4-dioxo-6-[(pyridin-4-y]methy])carbamoy]]-1.4-dihydro-2H-
quinazolin-3-yl]methyl]phenyl]acetic acid
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
(Uses)
   (MMP13 inhibitor: preparation of quinazolines as specific inhibitors of
   type-13 matrix metalloprotease)
4315-09-7P, 4-Nitroisophthalic acid
                                     23965-06-2P, 3-Benzyl-6-bromo-1H-
quinazoline-2,4-dione 33857-88-4P 63746-12-3P, Dimethyl
4-aminoisophthalate 69048-70-0P. Dimethyl 4-nitroisophthalate
69209-73-0P 151979-21-4P. 5-Iodo-2-((methyl)amino)benzoic acid
177913-48-3P. Dimethyl 4-amino-1-hydroxycyclohexa-3,5-diene-1.3-
dicarboxylate 184681-83-2P. 1.3-Dimethyl-2,4-dioxo-1.2.3.4-
tetrahydropyrido[2.3-d]pyrimidine-6-carboxylic acid 209604-61-5P.
3-Benzyl-2.4-dioxo-1.2.3.4-tetrahydroquinazoline-6-carboxylic acid methyl
ester 221540-53-0P. 3-(4-Methoxybenzyl)-2.4-dioxo-1.2.3.4-
tetrahydroquinazoline-6-carboxylic acid methyl ester 342644-48-8P.
3-Benzyl-1-methyl-2.4-dioxo-1.2.3.4-tetrahydropyrido[2.3-d]pyrimidine-6-
carboxylic acid ethyl ester 449207-91-4P. 3-Benzyl-2.4-dioxo-1.2.3.4-
tetrahydroquinazoline-6-carboxylic acid 449207-92-5P 449207-93-6P.
3-Benzyl-2.4-dioxo-1.2.3.4-tetrahydroquinazoline-6-carbonitrile
449207-94-7P. 3-Benzyl-1-methyl-2.4-dioxo-1.2.3.4-tetrahydroquinazoline-6-
carboxylic acid 449207-95-8P, 3-Benzyl-1-methyl-2,4-dioxo-1,2,3,4-
tetrahydroquinazoline-6-carboxylic acid methyl ester 449207-96-9P.
1-Methyl-3-(3-fluorobenzyl)-2,4-dioxo-1,2,3,4-tetrahydroquinazoline-6-
```

carboxylic acid 449207-97-0P, 3-(3-Fluorobenzyl)-2,4-dioxo-1,2,3,4tetrahydroguinazoline-6-carboxylic acid methyl ester 449207-98-1P. 1-Methyl-3-(3-fluorobenzyl)-2.4-dioxo-1.2,3.4-tetrahydroquinazoline-6carboxylic acid methyl ester 449207-99-2P. 1-Ethyl-3-(3-fluorobenzyl)-2.4-dioxo-1.2.3.4-tetrahydroquinazoline-6-carboxylic acid 449208-00-8P. 1-Ethyl-3-(3-fluorobenzyl)-2.4-dioxo-1.2.3.4-tetrahydroquinazoline-6carboxylic acid methyl ester 449208-17-7P, 2,4-Dioxo-3-phenethyl-1,2,3,4tetrahydroquinazoline-6-carboxylic acid methyl ester 449208-18-8P. 2.4-Dioxo-3-phenethyl-1.2.3.4-tetrahydroquinazoline-6-carboxylic acid 449208-19-9P, 2.4-Dioxo-3-phenethyl-1.2.3.4-tetrahydroquinazoline-6carboxylic acid [benzo[1,3]dioxol-5-ylmethyl]amide 449208-21-3P. 3-(4-Methoxybenzyl)-2.4-dioxo-1.2.3.4-tetrahydroquinazoline-6-carboxylic acid 449208-24-6P. 3-(4-Methoxybenzyl)-2,4-dioxo-1,2,3,4tetrahydroguinazoline-6-carboxylic acid (4-methoxybenzyl)amide 449208-27-9P, Dimethyl 4-(N'-((pyridin-4-yl)methyl)ureido)isophthalate 449208-29-1P. 2.4-Dioxo-3-((pyridin-4-yl)methyl)-1,2,3,4tetrahydroquinazoline-6-carboxylic acid methyl ester 449208-31-5P. 2,4-Dioxo-3-((pyridin-4-yl)methyl)-1,2,3,4-tetrahydroguinazoline-6carboxylic acid 449208-33-7P 449208-34-8P, 2,4-Dioxo-3-(thien-2ylmethyl)-1.2.3.4-tetrahydroquinazoline-6-carboxylic acid methyl ester 449208-35-9P, 2,4-Dioxo-3-(thien-2-ylmethyl)-1,2,3,4-tetrahydroquinazoline-6-carboxylic acid 449208-43-9P 449208-44-0P, 3-((Benzo[1,3]dioxol-5yl)methyl)-2,4-dioxo-1,2,3,4-tetrahydroquinazoline-6-carboxylic acid methyl ester 449208-45-1P, 3-((Benzo[1,3]dioxol-5-yl)methyl)-2,4-dioxo-1.2.3.4-tetrahydroquinazoline-6-carboxylic acid 449208-51-9P. 1-Methyl-2.4-dioxo-1.2.3.4-tetrahydroquinazoline-6-carboxylic acid methyl 449208-53-1P 449208-68-8P, 3-Benzyl-2,4-dioxo-1,2,3,4tetrahydropyrido[2,3-d]pyrimidine-6-carboxylic acid 449209-10-3P. 3-(4-Chlorosulfonylbenzyl)-1-methyl-2,4-dioxo-1,2,3,4tetrahydroquinazoline-6-carboxylic acid methyl ester 449209-11-4P. 3-(4-Dimethylsulfamoylbenzyl)-1-methyl-2,4-dioxo-1,2,3,4tetrahydroquinazoline-6-carboxylic acid methyl ester 449209-12-5P. 3-(4-Dimethylsulfamoylbenzyl)-1-methyl-2,4-dioxo-1,2,3,4tetrahydroguinazoline-6-carboxylic acid 449209-15-8P. 1-Methyl-3-(4-methylsulfamoylbenzyl)-2,4-dioxo-1,2,3,4tetrahydroquinazoline-6-carboxylic acid methyl ester 449209-50-1P. 2.4-Dioxo-1-methyl-3-(pyridin-4-ylmethyl)-1,2,3,4-tetrahydroquinazoline-6carboxylic acid methyl ester 449209-51-2P, 2.4-Dioxo-1-methyl-3-(pyridine-4-ylmethyl)-1,2,3,4-tetrahydroquinazoline-6-carboxylic acid 449209-55-6P, 3-(4-Methoxycarbonylbenzyl)-2.4-dioxo-1.2.3.4tetrahydroquinazoline-6-carboxylic acid benzyl ester 449209-57-8P. 3-(4-Methoxycarbonylbenzyl)-1-methyl-2,4-dioxo-1,2,3,4tetrahydroquinazoline-6-carboxylic acid benzyl ester 449209-58-9P. 3-(4-Methoxycarbonylbenzyl)-1-methyl-2,4-dioxo-1,2,3,4tetrahydroguinazoline-6-carboxylic acid 449209-73-8P. 1-Methyl-2,4-dioxo-1,2,3,4-tetrahydroquinazoline-6-carboxylic acid (pyridin-4-ylmethyl)amide 449210-02-0P. 1.3-Dimethyl-2.4-dioxo-1.2.3.4tetrahydropyrido[3,4-d]pyrimidine-6-carboxylic acid 449210-04-2P 449210-05-3P 449210-06-4P, 3-Benzyl-1-methyl-2,4-dioxo-1,2,3.4tetrahydropyrido[2.3-d]pyrimidine-6-carboxylic acid 449210-08-6P. 1-Methyl-2,4-dioxo-1,2,3,4-tetrahydropyrido[2,3-d]pyrimidine-6-carboxylic acid 449210-09-7P 449210-10-0P, Methyl 4-[[6-(4-Methoxybenzylcarbamoyl)-1-methyl-2,4-dioxo-1,4-dihydro-2H-pyrido[2,3d]pyrimidin-3-yl]methyl]benzoate 449210-14-4P. 1-Benzyl-2.6-dioxo-1.2.3.6-tetrahydropyrimidine-4-carboxaldehyde 449210-15-5P 449210-17-7P 449210-18-8P, 3-Benzyl-1-methyl-2,4-dioxo-1.2.3.4-tetrahydropyrido[3.4-d]pyrimidine-6-carboxylic acid methyl ester 449210-19-9P. 3-Benzyl-1-methyl-2.4-dioxo-1.2.3.4-tetrahydropyrido[3.4d]pyrimidine-6-carboxylic acid 449210-21-3P, 1-Methyl-2.4-dioxo-1.2.3.4tetrahydropyrido[3,4-d]pyrimidine-6-carboxylic acid 449210-22-4P 449210-25-7P 449210-26-8P. tert-Butyl 4-[[6-(3-Methoxybenzylcarbamoyl)-1methyl-2.4-dioxo-1.4-dihydro-2H-pyrido[3.4-d]pyrimidin-3yl]methyl]benzoate 449210-58-6P. 3-(4-Bromobenzyl)-2,4-dioxo-1,2,3,4tetrahydroquinazoline-6-carboxylic acid methyl ester 449210-59-7P.

```
1-Methyl-3-(4-bromobenzyl)-2.4-dioxo-1.2,3.4-tetrahydroquinazoline-6-
carboxylic acid methyl ester 449210-60-0P, 1-Methyl-3-(4-bromobenzyl)-
2.4-dioxo-1.2.3.4-tetrahydroquinazoline-6-carboxylic acid 449210-63-3P.
3-(3,4-Difluorobenzyl)-2,4-dioxo-1,2,3,4-tetrahydroquinazoline-6-
carboxylic acid methyl ester 449210-64-4P, 1-Methyl-3-(3.4-
difluorobenzyl)-2,4-dioxo-1,2,3,4-tetrahydroquinazoline-6-carboxylic acid
methyl ester 449210-65-5P, 1-Methyl-3-(3,4-difluorobenzyl)-2,4-dioxo-
1.2.3.4-tetrahydroquinazoline-6-carboxylic acid 449210-69-9P.
3-(3-Chloro-4-fluorobenzyl)-2.4-dioxo-1.2.3.4-tetrahydroquinazoline-6-
carboxylic acid methyl ester 449210-70-2P. 1-Methyl-3-(3-chloro-4-
fluorobenzyl)-2.4-dioxo-1.2.3.4-tetrahydroquinazoline-6-carboxylic acid
methyl ester 449210-71-3P, 1-Methyl-3-(3-chloro-4-fluorobenzyl)-2.4-
dioxo-1.2.3.4-tetrahydroquinazoline-6-carboxylic acid 449210-77-9P.
1-Methyl-2,4-dioxo-1,2,3,4-tetrahydroquinazoline-6-carboxylic acid
(pyridazin-4-ylmethyl)amide 449210-80-4P, 1-Methyl-2,4-dioxo-1.2,3.4-
tetrahydroquinazoline-6-carboxylic acid (pyridin-3-ylmethyl)amide
449210-83-7P 449210-86-0P, 1-Methyl-2,4-dioxo-1,2,3,4-
tetrahydroquinazoline-6-carboxylic acid ((2-methoxypyridin-4-
vl)methyl)amide 449210-91-7P. 3-Benzyl-6-iodo-1-methyl-1H-quinazoline-
2,4-dione
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
   (intermediate: preparation of quinazolines as specific inhibitors of type-13
   matrix metalloprotease)
9001-12-1, MMP-1 9004-06-2, MMP-12 79955-99-0, MMP 3 141256-52-2.
MMP 7 146480-35-5, MMP-2 146480-36-6, MMP-9 161384-17-4, MMP-14
175449-82-8. MMP-13
RL: BSU (Biological study, unclassified); BIOL (Biological study)
   (preparation of quinazolines as specific inhibitors of type-13 matrix
   metalloprotease)
78-73-9, Choline bicarbonate 78-77-3, Isobutyl bromide 79-07-2.
2-Chloroacetamide 96-32-2, Methyl bromoacetate 96-33-3, Methyl
acrylate 100-11-8, 4-Nitrobenzyl bromide 100-44-7, Benzyl chloride.
reactions 100-46-9, Benzylamine, reactions 100-51-6, Benzyl alcohol,
          104-84-7, 4-Methylbenzylamine 104-86-9, 4-Chlorobenzylamine
105-36-2, Ethyl bromoacetate 105-39-5, Ethyl 2-chloroacetate 106-95-6.
Allyl bromide, reactions 106-96-7. Prop-2-ynyl bromide 108-00-9.
N,N-Dimethylethylene diamine 108-01-0. 2-(Dimethylamino)ethanol
119-68-6. N-Methylanthranilic acid 138-39-6. 4-
(Aminomethyl)benzenesulfonamide 140-75-0, 4-Fluorobenzylamine
140-88-5, Ethyl acrylate 332-48-9, 2-(4-Fluorophenoxy)ethyl bromide
351-52-0, 4-Chloromethyl-2-fluoro-1-methoxybenzene 459-46-1 495-76-1.
Piperonyl alcohol 540-51-2, 2-Bromoethanol 586-95-8, 4-Pyridylcarbinol
593-71-5, Chloroiodomethane 622-78-6, Benzyl isothiocyanate 622-95-7.
4-Chlorobenzyl bromide 637-59-2, 3-Phenylpropyl bromide 870-63-3.
1-Bromo-3-methylbut-2-ene 874-89-5, 4-Hydroxymethylbenzonitrile
874-98-6, 3-(Bromomethyl)-1-methoxyphenyl 938-09-0, 2-Chloroethyl phenyl
sulfone 1117-71-1. Methyl 4-bromocrotonate 1129-28-8. Methyl
3-(bromomethyl)benzoate 1943-82-4, Phenethyl isocyanate 2144-37-8.
Methyl 5-(chloromethyl)-2-furoate 2393-23-9, 4-Methoxybenzylamine
2417-72-3. Methyl 4-(bromomethyl)benzoate 2550-36-9.
(Bromomethyl)cyclohexane 2620-50-0. Piperonylamine 2969-81-5. Ethyl
4-bromobutyrate 3113-72-2, 5-Methyl-2-nitrobenzoic acid 3173-56-6.
Benzyl isocyanate 3277-89-2. Phenethylmagnesium bromide
                                                          3395-91-3,
Methyl 3-bromopropanoate 3731-52-0, 3-(Aminomethyl)pyridine 3731-53-1,
4-Picolylamine 4070-48-8 4637-24-5 5071-96-5. 3-Methoxybenzylamine
5586-89-0 5794-88-7, 2-Amino-5-bromobenzoic acid 6232-11-7, Methyl
4-(aminomethyl)benzoate hydrochloride 6321-07-9, 4-Morpholin-4-
ylbutylamine 6482-24-2, 1-Bromo-2-methoxyethane 7005-47-2.
2-(Dimethylamino)-2-methylpropanol 7051-34-5. Cyclopropylmethyl bromide
7149-10-2, 4-Hydroxy-3-methoxybenzylamine hydrochloride 7398-42-7.
Methyl 4-(bromomethyl)phenylacetate 10406-25-4 13734-41-3
17201-43-3, 4-(Bromomethyl)benzonitrile 18469-52-8, Methyl 4-aminomethyl
benzoate 19059-68-8, 3-(Dimethylamino)-2,2-dimethylpropanol
```

```
22059-22-9, N-Hydroxyacetamidine 22600-30-2, Methyl 5-amino-2-furan
    carboxylate 25589-18-8. 3-Benzyl-6-methyl-1H-pyrimidine-2,4-dione
    26146-77-0, (E)-Cinnamyl bromide 27757-85-3, 2-Thienylmethylamine
    28188-41-2. 3-(Bromomethyl)benzonitrile 30260-66-3. Dimethylhydrazine
    30280-44-5. 4-Chlorobenzyl isocyanate 32863-31-3. 5-
    Bromomethylbenzofurazan 39077-96-8 40724-47-8. 4-
    Bromomethylbenzenesulfonamide 41886-04-8, 3-Bromomethyl-1-
    methylpiperidine 50541-93-0. 4-Amino-1-benzylpiperidine 55401-97-3.
    2-(Bromomethyl)pyridine 56651-60-6. 4-Methoxybenzyl isocyanate
    69966-55-8, 3-(Bromomethyl)pyridine 72235-53-1, 3,4-Difluorobenzylamine
    72235-56-4, 3-Chloro-4-fluorobenzylamine 74733-27-0, Methyl
    4-bromomethy1-2-methoxybenzoate 74733-28-1, Methyl 4-bromomethy1-2-
    methyl benzoate 78358-86-8. 1-(2-Bromoethyl)pyrrole 78826-46-7.
    (tert-Butoxy)acetyl chloride 83171-39-5, 4-Methylthiobenzylamine
    85070-57-1. Methyl 4-(bromomethyl)-2-fluorobenzoate 85147-14-4
    88442-63-1. 1-(1-Naphthyl)ethyl isocyanate 89583-07-3.
    4-(2-Bromoethyl)morpholine 93919-56-3, 4-Trifluoromethoxybenzylamine
    99067-96-6. (4-(Dimethylamino)benzyl)isocyanate 102422-56-0,
    3-Fluorobenzyl isocyanate 108052-76-2, tert-Butyl 4-bromomethylbenzoate
    108499-32-7. Methyl 5-bromomethylthiophene-2-carboxylate 114772-38-2
    114772-54-2. 2-(4-Bromomethylphenyl)benzonitrile 120788-70-7. Ethyl
    1.3-dimethyl-2.4-dioxo-1.2.3.4-tetrahydropyrido[2.3-d]pyrimidine-6-
    carboxylate 128674-45-3, 4-(3-Chloropropenyl)pyridine hydrochloride
                 138895-24-6, 6-Amino-3-benzyl-1H-pyrimidine-2.4-dione
    138402-33-2
    148900-69-0 154470-79-8. Methyl 1.3-dimethyl-2.4-dioxo-1.2.3.4-
    tetrahydropyrido[3.4-d]pyrimidine-6-carboxylate 155965-45-0
    220875-89-8. 5-(4-Chloromethylphenyl)-1-methyl-1H-tetrazole 221031-44-3.
    2-Chloro-1-(4-diethylaminophenyl)ethan-1-one 302912-23-8, 4-Bromobenzyl
    isocyanate 304873-96-9, tert-Butyl (5-bromomethylpyridin-2-yl)carbamate
    448965-87-5, tert-Butyl 1-(4-bromomethylphenyl)cyclopropanecarboxylate
    449208-54-2, 1-Methyl-2,4-dioxo-1,2,3,4-tetrahydroquinazoline-6-carboxylic
    acid 449209-03-4, 3-((E)-3-Chloropropenyl)pyridine 449209-05-6.
    4-((E)-3-Chloropropenyl)pyridine 449209-08-9, 3-(4-
    (Methanesulfonyl)benzyl)-1-methyl-2.4-dioxo-1.2.3.4-tetrahydroguinazoline-
    6-carboxylic acid 449209-35-2, 3-(4-Chloromethylphenyl)-5-
    methyl[1.2.4]oxadiazole 449209-38-5, Methyl 2-chloro-4-
    chloromethylbenzoate 449209-42-1. 5-(4-Chloromethylphenyl)-2-methyl-2H-
    tetrazole 449209-56-7
    RL: RCT (Reactant): RACT (Reactant or reagent)
       (reactant; preparation of quinazolines as specific inhibitors of type-13
       matrix metalloprotease)
             THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD
(1) Abou-Hadeed, K; PTERIDINES 1996, V7(4), P113 HCAPLUS
(2) Anon: AMBINTER: EXPLORATORY LIBRARY 2002
(3) Anon: CHEMSTAR PRODUCT LIST 2001
(4) Anon: SCIENTIFIC EXCHANGE PRODUCT LIST 2001
(5) Anon; SCREENING COLLECTION 2000
(6) Bemis, G: WO 9964400 A 1999 HCAPLUS
(7) Brittelli, D: WO 9743239 A 1997 HCAPLUS
(8) Chen, J; JOURNAL OF THE AMERICAN CHEMICAL SOCIETY 2000, V122, P9648 HCAPLUS
(9) Ciba Geigy Ag; DE 2441959 A 1975 HCAPLUS
(10) Ghose, A: J MED CHEM 1984, V27(7), P901 HCAPLUS
(11) Kim. Y: CHEMISTRY AND BIOLOGY OF PTERIDINES AND FOLATES 1997. PROCEEDINGS
   OF THE INTERNATIONAL SYMPOSIUM ON PTERIDINES AND FOLATES. 11TH 1997, P41
```

- (12) Lespagnol, A; BULL SOC PHARM LILLE 1977, V33(1), P67 HCAPLUS
- (13) Liverton, N; BIOORGANIC & MEDICINAL CHEMISTRY LETTERS 1998, V8(5), P483 HCAPLUS
- (14) Murata, S; CHEMISTRY AND BIOLOGY OF PTERIDINES AND FOLATES 1997, PROCEEDINGS OF THE INTERNATIONAL SYMPOSIUM ON PTERIDINES AND FOLATES. 11TH 1997, P17 HCAPLUS
- (15) Nesterov: SU 119879 A 1959 HCAPLUS

MEDI INF

(16) Ogawa, H: CHEM PHARM BULL 1988, V36(6), P2253 HCAPLUS

- (17) Reiter, L: BIOORGANIC & MEDICINAL CHEMISTRY LETTERS 1999, V9(2). P127
- (18) Sladowska, H: FARMACO, ED SCI 1986. V41(12), P954 HCAPLUS

=> b wpix

FILE 'WPIX' ENTERED AT 11:22:53 ON 07 FEB 2005 COPYRIGHT (C) 2005 THE THOMSON CORPORATION

FILE LAST UPDATED: 2 FEB 2005 <20050202/UP> MOST RECENT DERWENT UPDATE: <200508/DW> 200508 DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE. COVERS 1963 TO DATE

>>> FOR A COPY OF THE DERWENT WORLD PATENTS INDEX STN USER GUIDE. PLEASE VISIT:

http://www.stn-international.de/training_center/patents/stn_guide.pdf <<<

- >>> FOR DETAILS OF THE PATENTS COVERED IN CURRENT UPDATES, SEE <<< http://thomsonderwent.com/coverage/latestupdates/
- >>> FOR INFORMATION ON ALL DERWENT WORLD PATENTS INDEX USER GUIDES, PLEASE VISIT: http://thomsonderwent.com/support/userguides/
- >>> NEW! FAST-ALERTING ACCESS TO NEWLY-PUBLISHED PATENT DOCUMENTATION NOW AVAILABLE IN DERWENT WORLD PATENTS INDEX FIRST VIEW - FILE WPIFV. FOR FURTHER DETAILS: http://www.thomsonderwent.com/dwpifv <<<
- >>> NEW DISPLAY FORMAT HITSTR ADDED ALLOWING DISPLAY OF HIT STRUCTURES WITHIN THE BIBLIOGRAPHIC DOCUMENT <
- >>> SMILES and ISOSMILES strings are no longer available as Derwent Chemistry Resource display fields <<<
- >>> THE CPI AND EPI MANUAL CODES HAVE BEEN REVISED FROM UPDATE 200501. PLEASE CHECK:

http://thomsonderwent.com/support/dwpiref/reftools/classification/code-revision/ FOR DETAILS. <<<

=> d all 18

- L8 ANSWER 1 OF 1 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN
- AN 2002-740698 [80] WPIX DNC C2002-209675
- New quinazolines useful in the treatment of e.g. arthritis, multiple sclerosis, periodontal disease, inflammatory bowel disease, and psoriasis. are matrix metalloproteinase inhibitors.
- DC B02
- ANDRIANJARA. C: BARVIAN, N C; GAUDILLIERE. B; JACOBELLI, H: KOSTLAN, C R; IN ORTWINE, D F; PATT, W C: PHAM, L: WILSON, M W; CHANTEL-BARVIAN, N
- (WARN) WARNER LAMBERT CO LLC; (ANDR-I) ANDRIANJARA C; (BARV-I) BARVIAN N C; (GAUD-I) GAUDILLIERE B; (JACO-I) JACOBELLI H; (KOST-I) KOSTLAN C R; (ORTW-I) ORTWINE D F; (PATT-I) PATT W C; (PHAM-I) PHAM L; (WILS-I) WILSON M W: (WARN) WARNER LAMBERT CO

- WO 2002064572 A1 20020822 (200280)* EN 64 C07D239-96
 - RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZM ZW
 - W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM

```
C07D487-02
    US 2002193377
                    A1 20021219 (200303)
                                                                     <--
    NO 2003003593 A 20030813 (200373)
                                                      C07D239-96
    EP 1368324
                     A1 20031210 (200382) EN
                                                      C07D239-96
        R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT
            RO SE SI TR
                   A 20030919 (200409)
     KR 2003074827
                                                      C07D405-12
    HU 2003003164
                    A2 20040128 (200415)
                                                      C07D239-96
                                                      C07D239-96
    AU 2002253070
                    A1 20020828 (200427)
                    W 20040805 (200451)
                                               445
                                                      C07D239-96
    JP 2004523546
    SK 2003001001
                    A3 20040908 (200462)
                                                      C07D239-96
     CZ 2003002142
                   A3 20041215 (200501)
                                                      C07D239-96
                    A 20041013 (200508)
     CN 1537105
                                                      C07D239-96
ADT WO 2002064572 A1 WO 2002-EP1979 20020211; US 2002193377 A1
     Provisional US 2001-268661P 20010214, US 2002-75954 20020213; NO
     2003003593 A WO 2002-EP1979 20020211, NO 2003-3593 20030813; EP 1368324 A1
     EP 2002-722137 20020211, WO 2002-EP1979 20020211; KR 2003074827 A KR
     2003-710659 20030813; HU 2003003164 A2 WO 2002-EP1979 20020211. HU
     2003-3164 20020211: AU 2002253070 A1 AU 2002-253070 20020211: JP
     2004523546 W JP 2002-564505 20020211. WO 2002-EP1979 20020211: SK
     2003001001 A3 WO 2002-EP1979 20020211, SK 2003-1001 20020211: CZ
     2003002142 A3 WO 2002-EP1979 20020211, CZ 2003-2142 20020211; CN 1537105 A
     CN 2002-805014 20020211
FDT EP 1368324 A1 Based on WO 2002064572; HU 2003003164 A2 Based on WO
     2002064572; AU 2002253070 A1 Based on WO 2002064572; JP 2004523546 W Based
     on WO 2002064572: SK 2003001001 A3 Based on WO 2002064572: CZ 2003002142
     A3 Based on WO 2002064572
PRAI US 2001-268661P
                          20010214: US 2002-75954
     20020213
    ICM C07D239-96; C07D405-12; C07D487-02
     ICS A61K031-5025; A61K031-505; A61K031-517; A61K031-519; A61K031-525;
          A61K031-5377: A61P001-02; A61P001-04; A61P009-04; A61P009-10;
          A61P011-00; A61P011-06; A61P017-06; A61P019-00; A61P019-02;
          A61P019-10: A61P025-28: A61P027-02: A61P029-00: A61P035-00:
          A61P043-00; C07D239-72; C07D239-95; C07D401-06; C07D401-12;
          C07D403-10; C07D403-12; C07D405-06; C07D405-14; C07D409-06;
          CO7D409-12: CO7D409-14: CO7D410-10: CO7D413-06: CO7D413-10:
          C07D471-04
    WO 200264572 A UPAB: 20021212
     NOVELTY - Quinazolines are new.
          DETAILED DESCRIPTION - Quinazolines of formula (I), their racemic.
     isomers. N-oxides, or salts are new.
          R1 = H, amino, T, 3-6C alkenyl, 3-6C alkynyl, mono or di-T-amino-T.
     aryl. aryl-T, heterocycle, or 3-6 membered cycloalkyl-T (all optionally
     substituted by at least one amino, T. cyano, halo-T, C(0)OR4, OR4 or SR4);
     T = 1-6C \text{ alkyl}
     R4 = H \text{ or } T:
          W = 0, S, or a group NR';
          R' = T, hydroxyl, or cyano;
          X1 - X3 = N \text{ or } CR6:
          R6 = H. T. amino, mono or di-T-amino, hydroxyl, 1-6C alkoxy, or
     halo:
          Y = 0, S, NH, or N-T;
          Z = 0. S. or NR7:
          R7 = H. T. aryl-T. cycloalkyl. or (hetero)aryl:
     n = 1-8:
     Z1 = CR8R9:
          R8 and R9 = H. T. halo-T. halo. amino. OR4. SR4 or C(0)OR4:
          A = 5 or 6 membered optionally aromatic monocycle containing 0-4 N. O
     or S, or bicycle, composed of two aromatic or non-aromatic, 5 or 6
     membered rings, containing 0-4 N, O, or S;
          R2 = T. halogen, CN, NO2, SCF3, CF3, OCF3, NR10R11, OR10, SR10,
     SOR10, SO2R10, (CH2)kSO2NR10OR11, X5(CH2)kC(0)OR10, (CH2)kC(0)OR10.
```

```
X5(CH2)kC(0)NR10R11, (CH2)kC(0)NR10R11,X4R12;
     X5 and X7 = 0, or S optionally substituted by 1 or 2 0, or N
substituted by H or T;
k = 0-3:
     R10 and R11 = H or T:
     X4 and X6 = single bond, CH2, or X5:
     R12 = 5 or 6 membered ring (optionally substituted by at least one of
T, halo, hydroxyl and amino:
     R3 = H, T, 3-6C alkenyl, 3-6C alkynyl (optionally substituted by at
least one of amino, cyano, halo-T, cycloalkyl, C(=0)NR10R11, C(=0)0R10,
OR10, and SR10;
     R10 and R11 = H. T. or (R5)-B-(Z2)p:
p = 0-8:
Z2 = CR13R14;
     R13 and R14 = H. T. phenyl, halo-T. halo, amino, OR4, SR4 or
C(=0)0R4:
     R4 and R15 - R17 = H or T,
     B = 5 or 6 membered monocycle containing 0-4 N O, or S, bicycle.
composed of 5 or 6 membered rings containing 0-4 N, O, or S;
     R5 = T, halogen, CN, NO2, CF3, OCF3, (CH2)kNR15R16, N(R15)C(O)R16.
N(R15)C(0)OR16, N(R15)SO2R16, N(SO2R1)R15)2, OR15, S(0)k1R15, SO2NR16R17,
(CH2)k2NR15R16, (CH2)kSQ2NR15R16, X7(CH2)kC(0)OR15, (CH2)kC(0)OR16.
C(0)O(CH2)k2NR15R16, C(0)O(CH2)k2C(0)OR18, X7(CH2)kC(0)NR15R16.
(CH2)kC(0)NR15R16, R19C(0)OR15, X6R20, or C(0)-R21NR15R16;
k = 0-3;
k1 = 0-2:
k2 = 1-4:
     R18 = 1-6C \text{ alkyl}, R21NR15R16, -R21R15C(0)R21NR15R16, or
C(0)0R21NR15R16;
     R21 = 1-6C alkylene group;
     R19 = 3-6C cycloalkyl group;
     R20 = 5 or 6 membered ring (optionally substituted by at least one of
1-6C alkyl, halo, OH, oxo, cyano, tetrazole, amino, and C(0)OR4.
Provided that:
     (1) When n at least 2 then the hydrocarbon chain Z1 and Z2 optionally
contains at least one multiple bond and/or one of the carbon atoms in the
hydrocarbon chain Z1 and Z2 may be replaced with X5;
     (2) When one of the carbon atoms in the hydrocarbon chain Z1 is
replaced with S (optionally substituted by 1 or 2 0), then the group
C(=Y)Z optionally may be absent in (I):
     (3) R12 is heterocyclic ring then it contains 1-4 of S, O, or N; and
     (4) when X1 is N, then X2 is other than a carbon atom substituted
with a methyl group or NH-CH3.
     INDEPENDENT CLAIMS are included for the following:
     (a) Intermediate of formulae (III) or (IV); and
     (b) Six methods for the preparations of (I).
     ACTIVITY - Antirheumatic; Antiarthritic: Osteopathic:
Antiinflammatory: Psoriatic: Neuroprotective: Cardiant:
Antiarteriosclerotic; Asthmatic; Cytostatic.
     MECHANISM OF ACTION - Matrix metalloprotease (MMP)-13 inhibitor.
     A reaction contained (4-(2-hydroxyethyl)-1-piperazine ethane sulfonic
acid (50 mM), CaCl2 (10 mM), pH 7, room temperature, 5.5'-dithiobis(2-
nitrobenzoic acid) (DTNB) (1 mM), thiopeptolide substrate
Ac-Pro-Leu-Gly-thioester-Leu-Leu-Gly. Ethanol (100 micro M), inhibitor in
2% dimethylsulfoxide and human collagenase-3 catalytic domain enzyme (2.5
nM). 4(6-(4-Methoxy-benzylcarbamoyl)-methyl-2,4-dioxo-1,4-dihydro-2H-
quinazolin-3-ylmethyl)-benzoate (A) was screened from 100 micro M - 0.5
nM. The change in the absorbance at 405 nm was monitored on microplate
reader at room temperature for 10-15 minutes. (A) showed IC50 value 0.001
micro M.
     USE - In the preparation of medical product for treating a disease or
```

therapy involving inhibition of type-13 matrix metalloprotease e.g. arthritis, rheumatoid arthritis, osteoarthritis, osteoporosis, periodontal

disease, inflammatory bowel disease, psoriasis, multiple sclerosis, cardiac insufficiency, atherosclerosis, asthma, chronic obstructive pulmonary disease, age related muscular degeneration and cancer (all claimed).

ADVANTAGE - (I) have selective and high inhibition activity for matrix metalloprotease-13.

Dwg.0/0

FS CPI

FA AB: GI: DCN

MC CPI: B06-H; B14-C09; B14-D07C; B14-E10C; B14-F01; B14-F07; B14-H01; B14-K01; B14-N01; B14-N03; B14-N06B; B14-N17; B14-S01

=> b home

FILE 'HOME' ENTERED AT 11:23:05 ON 07 FEB 2005

=>

=> b reg

FILE 'REGISTRY' ENTERED AT 11:47:06 ON 07 FEB 2005 USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT. PLEASE SEE "HELP USAGETERMS" FOR DETAILS. COPYRIGHT (C) 2005 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 6 FEB 2005 HIGHEST RN 826990-02-7 DICTIONARY FILE UPDATES: 6 FEB 2005 HIGHEST RN 826990-02-7

TSCA INFORMATION NOW CURRENT THROUGH MAY 21, 2004

Please note that search-term pricing does apply when conducting ${\tt SmartSELECT}$ searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at: http://www.cas.org/ONLINE/DBSS/registryss.html

=> d que sta 115

L13

VAR G1=N/O/S REP G2=(0-1) AK NODE ATTRIBUTES: DEFAULT MLEVEL IS ATOM DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES: RING(S) ARE ISOLATED OR EMBEDDED NUMBER OF NODES IS 19

STEREO ATTRIBUTES: NONE

L15 7 SEA FILE=REGISTRY SSS FUL L13

100.0% PROCESSED 31 ITERATIONS

7 ANSWERS

SEARCH TIME: 00.00.01

=> d his

(FILE 'HOME' ENTERED AT 11:20:28 ON 07 FEB 2005)

FILE 'HCAPLUS' ENTERED AT 11:20:35 ON 07 FEB 2005

L1 1 US20020193377/PN

E US2001-268661/AP.PRN

L2 1 US2001-268661P/AP.PRN

L3 1 L1-2

FILE 'REGISTRY' ENTERED AT 11:21:44 ON 07 FEB 2005

Page 2

```
FILE 'HCAPLUS' ENTERED AT 11:21:46 ON 07 FEB 2005
L4
                TRA L3 1- RN :
                                     441 TERMS
     FILE 'REGISTRY' ENTERED AT 11:21:48 ON 07 FEB 2005
L5
            441 SEA L4
     FILE 'WPIX' ENTERED AT 11:21:54 ON 07 FEB 2005
L6
              1 US20020193377/PN
              1 US2001-268661P/AP.PRN
L7
                E US2001-268661/AP.PRN
L8
              1 L6-7
     FILE 'REGISTRY' ENTERED AT 11:35:05 ON 07 FEB 2005
L9
                STR
L10
              0 L9
                STR L9
L11
              0 L11
112
L13
                STR L11
L14
              0 L13
              7 L13 FULL
L15
                SAV TEM L15 TRU954F0/A
     FILE 'HCAPLUS' ENTERED AT 11:45:42 ON 07 FEB 2005
116
              4 1 1 5
     FILE 'HCAOLD' ENTERED AT 11:45:49 ON 07 FEB 2005
L17
              0 L15
=> b hcap
FILE 'HCAPLUS' ENTERED AT 11:47:20 ON 07 FEB 2005
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
```

Copyright of the articles to which records in this database refer is held by the publishers listed in the PUBLISHER (PB) field (available for records published or updated in Chemical Abstracts after December 26, 1996), unless otherwise indicated in the original publications. The CA Lexicon is the copyrighted intellectual property of the the American Chemical Society and is provided to assist you in searching databases on STN. Any dissemination, distribution, copying, or storing of this information, without the prior written consent of CAS, is strictly prohibited.

FILE COVERS 1907 - 7 Feb 2005 VOL 142 ISS 7 FILE LAST UPDATED: 6 Feb 2005 (20050206/ED)

COPYRIGHT (C) 2005 AMERICAN CHEMICAL SOCIETY (ACS)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d all hitstr 116 1-2

```
L16 ANSWER 1 OF 4 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 2004:60320 HCAPLUS

DN 140:105336

ED Entered STN: 26 Jan 2004

TI Combination of an allosteric carboxylic inhibitor of matrix metalloproteinase-13 with a selective inhibitor of cyclooxygenase-2 that is not celecoxib or valdecoxib, and therapeutic use

IN Roark, William Howard

PA Warner-Lambert Company LLC, USA
```

```
S0
    PCT Int. Appl., 239 pp.
    CODEN: PIXXD2
DT
    Patent
LA
    English
IC
    ICM A61K031-519
    ICS A61K031-00; A61P019-02; A61P009-00
    1-12 (Pharmacology)
FAN.CNT 1
    PATENT NO.
                        KIND DATE
                                            APPLICATION NO.
                                                                   DATE
                               -----
                        ----
                               20040122
                                            WO 2003-IB3098
                                                                   20030707
    WO 2004006931
                         A2
    WO 2004006931
                         A3
                               20040513
        W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH.
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,
             PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT,
             TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY.
             KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES.
             FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
             BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
    US 2004019054
                         A1
                               20040129
                                           US 2003-619769
PRAI US 2002-396785P
                         Р
                               20020717
CLASS
                CLASS PATENT FAMILY CLASSIFICATION CODES
 PATENT NO.
 WO 2004006931 ICM
                       A61K031-519
                       A61K031-00: A61P019-02: A61P009-00
                ICS
    MARPAT 140:105336
    The invention provides a combination comprising an allosteric carboxylic
     inhibitor of MMP-13, or a pharmaceutically acceptable salt thereof, with a
     selective inhibitor of COX-2, or a pharmaceutically acceptable salt
    thereof, that is not celecoxib or valdecoxib, and their use for the
     treatment of diseases that are responsive to inhibition of MMP-13 and
    cyclooxygenase-2.
   cyclooxygenase 2 inhibitor MMP13 allosteric carboxylic inhibitor
    combination therapeutic: matrix metalloproteinase 13 inhibitor
    cyclooxygenase 2 inhibitor combination therapeutic
    Ampuls.
    Analgesics
    Anti-inflammatory agents
    Antiarthritics
     Antirheumatic agents
     Drug delivery systems
     Inflammation
    Osteoarthritis
    Pain
     Rheumatoid arthritis
        (allosteric carboxylic inhibitor of matrix metalloproteinase-13
        combination with selective inhibitor of cyclooxygenase-2 that is not
        celecoxib or valdecoxib, and therapeutic use)
    Drug delivery systems
        (capsules: allosteric carboxylic inhibitor of matrix
        metalloproteinase-13 combination with selective inhibitor of
        cyclooxygenase-2 that is not celecoxib or valdecoxib. and therapeutic
        use)
    Cartilage, disease
        (damage; allosteric carboxylic inhibitor of matrix metalloproteinase-13
        combination with selective inhibitor of cyclooxygenase-2 that is not
        celecoxib or valdecoxib, and therapeutic use)
    Drug delivery systems
        (injections; allosteric carboxylic inhibitor of matrix
        metalloproteinase-13 combination with selective inhibitor of
```

cyclooxygenase-2 that is not celecoxib or valdecoxib, and therapeutic use)

IT Drug delivery systems

(ointments: allosteric carboxylic inhibitor of matrix metalloproteinase-13 combination with selective inhibitor of cyclooxygenase-2 that is not celecoxib or valdecoxib, and therapeutic use)

IT Drug delivery systems

(solns.: allosteric carboxylic inhibitor of matrix metalloproteinase-13 combination with selective inhibitor of cyclooxygenase-2 that is not celecoxib or valdecoxib, and therapeutic use)

IT Drug delivery systems

(suppositories: allosteric carboxylic inhibitor of matrix metalloproteinase-13 combination with selective inhibitor of cyclooxygenase-2 that is not celecoxib or valdecoxib, and therapeutic use)

IT Drug delivery systems

(tablets. coated: allosteric carboxylic inhibitor of matrix metalloproteinase-13 combination with selective inhibitor of cyclooxygenase-2 that is not celecoxib or valdecoxib, and therapeutic use)

IT Drug delivery systems

(tablets: allosteric carboxylic inhibitor of matrix metalloproteinase-13 combination with selective inhibitor of cyclooxygenase-2 that is not celecoxib or valdecoxib, and therapeutic use)

IT 175449-82-8, Matrix metalloproteinase 13 329900-75-6. Cyclooxygenase 2 RL: BSU (Biological study, unclassified); BIOL (Biological study) (allosteric carboxylic inhibitor of matrix metalloproteinase-13 combination with selective inhibitor of cyclooxygenase-2 that is not celecoxib or valdecoxib, and therapeutic use)

IT 449210-07-5 449210-13-3 449210-20-2 449210-24-6 449210-27-9 449210-47-3

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL

(Biological study): USES (Uses)

(allosteric carboxylic inhibitor of matrix metalloproteinase-13 combination with selective inhibitor of cyclooxygenase-2 that is not celecoxib or valdecoxib. and therapeutic use)

IT 449210-13-3 449210-20-2 449210-24-6 449210-27-9 449210-47-3

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(allosteric carboxylic inhibitor of matrix metalloproteinase-13 combination with selective inhibitor of cyclooxygenase-2 that is not celecoxib or valdecoxib, and therapeutic use)

RN 449210-13-3 HCAPLUS

CN Pyrido[3.4-d]pyrimidine-6-carboxamide, N-(1.3-benzodioxol-5-ylmethyl)-1,2,3,4-tetrahydro-1-methyl-2,4-dioxo-3-(phenylmethyl)- (9CI) (CA INDEX NAME)

RN 449210-20-2 HCAPLUS

CN Benzoic acid. 4-[[1.4-dihydro-6-[[[(4-methoxyphenyl)methyl]amino]carbonyl]1-methyl-2.4-dioxopyrido[3.4-d]pyrimidin-3(2H)-yl]methyl]-. methyl ester
(9CI) (CA INDEX NAME)

RN 449210-24-6 HCAPLUS

CN Benzoic acid. 4-[[1.4-dihydro-6-[[[(3-methoxyphenyl)methyl]amino]carbonyl]1-methyl-2.4-dioxopyrido[3.4-d]pyrimidin-3(2H)-yl]methyl]- (9CI) (CA
INDEX NAME)

RN 449210-27-9 HCAPLUS

CN Pyrido[3,4-d]pyrimidine-6-carboxamide. 3-[(4-cyanophenyl)methyl]-1.2.3.4-tetrahydro-N-[(4-methoxyphenyl)methyl]-1-methyl-2.4-dioxo- (9CI) (CA INDEX NAME)

RN 449210-47-3 HCAPLUS

CN Benzoic acid. 4-[[1.4-dihydro-6-[[[(4-methoxyphenyl)methyl]amino]carbonyl]1-methyl-2.4-dioxopyrido[3.4-d]pyrimidin-3(2H)-yl]methyl]- (9CI) (CA
INDEX NAME)

- L16 ANSWER 2 OF 4 HCAPLUS COPYRIGHT 2005 ACS on STN
- AN 2004:60302 HCAPLUS
- DN 140:105333
- ED Entered STN: 26 Jan 2004
- TI Combination of an allosteric carboxylic inhibitor of matrix metalloproteinase-13 with celecoxib or valdecoxib, pharmaceutical compositions, and therapeutic use
- IN Roark, William Howard
- PA Warner-Lambert Company LLC, USA
- SO PCT Int. Appl., 238 pp. CODEN: PIXXD2
- DT Patent

```
LA
    English
IC
    ICM A61K031-415
     ICS A61K031-44: A61K031-42: A61K031-519
    1-12 (Pharmacology)
     Section cross-reference(s): 63
FAN.CNT 1
                                           APPLICATION NO.
                                                                   DATE
    PATENT NO.
                      · KIND
                               DATE
                                            ......
                                                                   20030707
                                20040122
                                           WO 2003-IB3044
ΡŢ
    WO 2004006912
                          A2
                               20040603
    WO 2004006912
                         A3
        W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH.
            GM. HR. HU. ID. IL. IN. IS. JP. KE. KG. KP. KR. KZ. LC. LK. LR.
            LS. LT. LU, LV. MA. MD, MG. MK. MN, MW. MX. MZ. NI. NO. NZ. OM.
             PH. PL. PT. RO. RU. SC. SD. SE. SG. SK. SL. TJ. TM. TN. TR. TT. TZ. UA. UG. US. UZ. VC. VN. YU. ZA. ZM. ZW
         RW: GH. GM, KE. LS. MW. MZ, SD, SL. SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
             KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
            FI. FR. GB. GR. HU, IE, IT, LU. MC. NL. PT. RO, SE, SI, SK, TR.
             BF. BJ. CF. CG. CI. CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
                                           US 2003-619662
                                20040129
     US 2004019053
                          A1
                                20020717
PRAI US 2002-396903P
                          Р
CLASS
                 CLASS PATENT FAMILY CLASSIFICATION CODES
 PATENT NO.
                       _____
 WO 2004006912
                ICM
                       A61K031-415
                       A61K031-44; A61K031-42; A61K031-519
                 ICS
    MARPAT 140:105333
   The invention provides a combination comprising an allosteric carboxylic
AR
     inhibitor of MMP-13, or a pharmaceutically acceptable salt thereof, with
     celecoxib, or a pharmaceutically acceptable salt thereof, or valdecoxib,
     or a pharmaceutically acceptable salt thereof. The invention also
     provides a method of treating a disease that is responsive to inhibition
     of MMP-13 and cyclooxygenase 2, comprising administering to a patient
     suffering from such a disease the invention combination comprising an
     allosteric carboxylic inhibitor of MMP-13, or a pharmaceutically
     acceptable salt thereof, with celecoxib, or a pharmaceutically acceptable
     salt thereof, or valdecoxib, or a pharmaceutically acceptable salt
     thereof. The invention also provides a pharmaceutical composition, comprising
     the invention combination comprising an allosteric carboxylic inhibitor of
     MMP-13, or a pharmaceutically acceptable salt thereof, with celecoxib, or
     a pharmaceutically acceptable salt thereof, or valdecoxib, or a
     pharmaceutically acceptable salt thereof, and a pharmaceutically
     acceptable carrier, diluent, or excipient. The invention combination may
     also be further combined with other pharmaceutical agents depending on the
     disease being treated.
     allosteric carboxylic inhibitor matrix metalloproteinase 13 celecoxib
     valdecoxib therapeutic; MMP13 allosteric carboxylic inhibitor celecoxib
     valdecoxib combination therapeutic
IT Ampuls
     Analgesics
     Anti-inflammatory agents
     Antiarthritics
     Antirheumatic agents
     Drug delivery systems
     Human
     Inflammation
     Osteoarthritis
     Pain
     Rheumatoid arthritis
        (allosteric carboxylic inhibitor of matrix metalloproteinase-13
        combination with celecoxib or valdecoxib, pharmaceutical compns., and
        therapeutic use)
```

Drug delivery systems

```
(capsules: allosteric carboxylic inhibitor of matrix
    metalloproteinase-13 combination with celecoxib or valdecoxib.
    pharmaceutical compns., and therapeutic use)
Cartilage, disease
    (damage; allosteric carboxylic inhibitor of matrix metalloproteinase-13
    combination with celecoxib or valdecoxib, pharmaceutical compns., and
    therapeutic use)
 Drug delivery systems
    (injections; allosteric carboxylic inhibitor of matrix
    metalloproteinase-13 combination with celecoxib or valdecoxib.
    pharmaceutical compns., and therapeutic use)
 Drug delivery systems
    (ointments; allosteric carboxylic inhibitor of matrix
    metalloproteinase-13 combination with celecoxib or valdecoxib,
    pharmaceutical compns., and therapeutic use)
Arthritis
    (psoriatic arthritis: allosteric carboxylic inhibitor of matrix
    metalloproteinase-13 combination with celecoxib or valdecoxib.
    pharmaceutical compns., and therapeutic use)
 Drug delivery systems
    (solns.; allosteric carboxylic inhibitor of matrix metalloproteinase-13
    combination with celecoxib or valdecoxib, pharmaceutical compns., and
    therapeutic use)
Drug delivery systems
    (suppositories: allosteric carboxylic inhibitor of matrix
    metalloproteinase-13 combination with celecoxib or valdecoxib.
    pharmaceutical compns., and therapeutic use)
 Drug delivery systems
    (tablets, coated; allosteric carboxylic inhibitor of matrix
    metalloproteinase-13 combination with celecoxib or valdecoxib.
    pharmaceutical compns., and therapeutic use)
 Drug delivery systems
    (tablets: allosteric carboxylic inhibitor of matrix
    metalloproteinase-13 combination with celecoxib or valdecoxib.
    pharmaceutical compns., and therapeutic use)
175449-82-8. Matrix metalloproteinase 13
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
    (allosteric carboxylic inhibitor of matrix metalloproteinase-13
    combination with celecoxib or valdecoxib, pharmaceutical compns., and
    therapeutic use)
169590-42-5, Celecoxib 181695-72-7, Valdecoxib 449210-07-5
 449210-13-3 449210-20-2 449210-24-6
 449210-27-9 449210-47-3
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
 (Biological study); USES (Uses)
    (allosteric carboxylic inhibitor of matrix metalloproteinase-13
    combination with celecoxib or valdecoxib, pharmaceutical compns., and
    therapeutic use)
 449210-13-3 449210-20-2 449210-24-6
 449210-27-9 449210-47-3
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
 (Biological study); USES (Uses)
    (allosteric carboxylic inhibitor of matrix metalloproteinase-13
    combination with celecoxib or valdecoxib, pharmaceutical compns., and
    therapeutic use)
449210-13-3 HCAPLUS
```

Pyrido[3,4-d]pyrimidine-6-carboxamide. N-(1,3-benzodioxol-5-ylmethyl)-1,2,3,4-tetrahydro-1-methyl-2,4-dioxo-3-(phenylmethyl)- (9CI) (CA INDEX

RN 449210-20-2 HCAPLUS

CN Benzoic acid. 4-[[1.4-dihydro-6-[[[(4-methoxyphenyl)methyl]amino]carbonyl]1-methyl-2,4-dioxopyrido[3,4-d]pyrimidin-3(2H)-yl]methyl]-. methyl ester
(9CI) (CA INDEX NAME)

RN 449210-24-6 HCAPLUS

CN Benzoic acid, 4-[[1.4-dihydro-6-[[[(3-methoxyphenyl)methyl]amino]carbonyl]1-methyl-2,4-dioxopyrido[3,4-d]pyrimidin-3(2H)-yl]methyl]- (9CI) (CA
INDEX NAME)

RN 449210-27-9 HCAPLUS

CN Pyrido[3,4-d]pyrimidine-6-carboxamide. 3-[(4-cyanophenyl)methyl]-1.2,3.4-tetrahydro-N-[(4-methoxyphenyl)methyl]-1-methyl-2,4-dioxo- (9CI) (CA INDEX NAME)

RN 449210-47-3 HCAPLUS

CN Benzoic acid. 4-[[1.4-dihydro-6-[[[(4-methoxyphenyl)methyl]amino]carbonyl]1-methyl-2,4-dioxopyrido[3,4-d]pyrimidin-3(2H)-yl]methyl]- (9CI) (CA
INDEX NAME)

```
=> d all fhitstr 116 3-4
L16 ANSWER 3 OF 4 HCAPLUS COPYRIGHT 2005 ACS on STN
AN
     2002:637660 HCAPLUS
DN
     137:185501
     Entered STN: 23 Aug 2002
FD
     Preparation of guinazolines as specific inhibitors of type-13 matrix
     Andrianjara, Charles: Chantel-Barvian, Nicole: Gaudilliere, Bernard:
     Jacobelli, Henri; Ortwine, Daniel Fred; Patt, William Chester; Pham, Ly;
     Kostlan, Catherine Rose; Wilson, Michael William
     Warner-Lambert Company, USA
S0
     PCT Int. Appl., 264 pp.
     CODEN: PIXXD2
DT
     Patent
     English
LA
IC
     ICM C07D239-96
     ICS C07D401-12; C07D405-12; C07D409-12; C07D405-14; C07D409-14;
          C07D471-04; C07D403-12; C07D403-10; C07D410-10; C07D413-10;
          C07D401-06: A61K031-5025: A61K031-505
     28-16 (Heterocyclic Compounds (More Than One Hetero Atom))
     Section cross-reference(s): 1
FAN.CNT 1
                                            APPLICATION NO.
                                                                    DATE
     PATENT NO.
                         KIND DATE
     . . . . . . . . . . . . . . . .
                         ----
                                -----
                                             _____
                                20020822
                                            WO 2002-EP1979
                                                                    20020211
                          Α1
PΤ
     WO 2002064572
         W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
             PL. PT. RO. RU. SD. SE, SG, SI. SK, SL, TJ. TM, TN, TR. TT, TZ.
             UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU,
             TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,
             BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
                          AA 20020822 CA 2002-2437122
                                                                    20020211
     CA 2437122
     EP 1368324
                                20031210
                                             EP 2002-722137
                          A1
         R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
                                20031215
                                             EE 2003-384
                                                                    20020211
     EE 200300384
                          Α
                                             JP 2002-564505
                                                                    20020211
     JP 2004523546
                          T2
                                20040805
     US 2002193377
                         · A1
                                20021219
                                             US 2002-75954
                                                                    20020213
     NO 2003003593
                          Α
                                 20030813
                                             NO 2003-3593
                                                                    20030813
                          Р
PRAI US 2001-268661P
                                20010214
     WO 2002-EP1979
                          W
                                 20020211
CLASS
                 CLASS PATENT FAMILY CLASSIFICATION CODES
 PATENT NO.
 ------
 WO 2002064572
                 ICM
                        C07D239-96
                        C07D401-12; C07D405-12; C07D409-12; C07D405-14;
                 ICS
                        C07D409-14: C07D471-04: C07D403-12: C07D403-10:
                        C07D410-10: C07D413-10: C07D401-06; A61K031-5025:
                        A61K031-505
                 FTERM 4C063/AA01: 4C063/AA03: 4C063/BB03: 4C063/BB06:
 JP 2004523546
                        4C063/BB08: 4C063/BB09: 4C063/CC31: 4C063/CC47:
                        4C063/CC58; 4C063/CC81; 4C063/CC92; 4C063/DD12;
                        4C063/DD28: 4C063/DD31: 4C063/EE01: 4C065/AA04;
                        4C065/AA05; 4C065/BB11; 4C065/CC01; 4C065/DD03;
                        4C065/EE02: 4C065/HH08: 4C065/JJ01: 4C065/KK01:
                         4C065/KK09: 4C065/LL04: 4C065/PP03: 4C065/PP07;
```

```
4C065/PP12: 4C065/QQ04: 4C065/QQ05: 4C086/AA01: 4C086/AA02: 4C086/AA03: 4C086/AA04: 4C086/BC46: 4C086/BC62: 4C086/BC71: 4C086/BC73: 4C086/CB09: 4C086/GA07: 4C086/GA08: 4C086/GA09: 4C086/GA12: 4C086/MA01: 4C086/MA02: 4C086/MA03: 4C086/MA04: 4C086/MA05: 4C086/NA04: 4C086/ZA15: 4C086/ZA33: 4C086/ZA36: 4C086/ZA45: 4C086/ZA67: 4C086/ZA68: 4C086/ZA96: 4C086/ZA97: 4C086/ZB15: 4C086/ZB26: 4C086/ZC20: 4C086/ZC41: 4C086/ZC52
```

OS CASREACT 137:185501; MARPAT 137:185501

GI

Title compds. I [R1 = H, amino, alkyl, alkenyl, alkynyl, alkylamino, aryl, heterocycle, etc.; W = O, S, =N-R'; R' = alkyl, OH, CN; X1-3 = N, C-R6; R6 = H. alkyl, amino, alkylamino, etc.; Y = O, S, NH, N-alkyl; Z = O, S, NR7; R7 = H, alkyl, aryl, heteroaryl, etc.; n = 1-8; Z1 = alkyl; A = 1-8(non)aromatic, 5- or 6-membered monocycle comprising from 0 to 4 heteroatoms selected from N. O. S. etc.; m = 0-7; R2 = alkyl, halo, CN, NO2, SCF3. CF3, OCF3, etc.; R3 = H, alkyl, alkenyl, alkynyl, etc.] were prepared Over 200 synthetic examples were provided. For instance, di-Me 4-aminoisophthalate was reacted with benzylisocyanate and heated to 95-100.degree. overnight to give Me 3-benzyl-2.4-dioxo-1,2.3,4tetrahydroquinazoline-6-carboxylate which was saponified (dioxaneaq, LiOH, reflux) to give the carboxylic acid. This intermediate was coupled with benzylamine to afford II. Selected examples of I had IC50 = 2.25 - 0.001.mu.M for MMP13 and IC50 > 100 .mu.M for MMP1, MMP2, MMP3, MMP7, MMP9. MMP12 and MMP14; II had IC50 = 0.193 .mu.M for MMP13. Compds. I are useful for the treatment of osteoarthritis and rheumatoid arthritis.

ST quinazoline mmp matrix metalloprotease inhibitor prepn

IT Antiarteriosclerotics

(antiatherosclerotics; preparation of quinazolines as specific inhibitors of type-13 matrix metalloprotease)

IT Lung, disease

(chronic obstructive: preparation of quinazolines as specific inhibitors of type-13 matrix metalloprotease)

IT Heart, disease

IT Intestine, disease

IT Eye, disease

(macula, senile degeneration; preparation of quinazolines as specific inhibitors of type-13 matrix metalloprotease)

IT Antiarthritics

```
Antiasthmatics
       Antirheumatic agents
       Antitumor agents
       Arthritis
       Asthma
       Atherosclerosis
       Human
       Multiple sclerosis
       Neoplasm
       Osteoarthritis
       Osteoporosis
       Periodontium. disease
       Psoriasis
       Rheumatoid arthritis
            (preparation of guinazolines às specific inhibitors of type-13 matrix
            metalloprotease)
IT Multiple sclerosis
       Osteoporosis
            (therapeutic agents: preparation of guinazolines as specific inhibitors of
            type-13 matrix metalloprotease)
     449208-02-0P, 3-Benzyl-2,4-dioxo-1,2,3,4-tetrahydroquinazoline-6-
       carboxylic acid (4-pyridylmethyl)amide 449208-14-4P 449208-50-8P.
       1-Methyl-2,4-dioxo-1,2,3,4-tetrahydroguinazoline-6-carboxylic acid
       [benzo[1,3]dioxol-5-ylmethyl]amide 449208-52-0P, Methyl
       4-[[6-(4-methoxybenzylcarbamoyl)-1-methyl-2,4-dioxo-1,4-dihydro-2H-
       quinazolin-3-yl]methyl]benzoate 449208-55-3P. 4-[[6-(4-
       Methoxybenzylcarbamoyl)-1-methyl-2,4-dioxo-1,4-dihydro-2H-quinazolin-3-
       yl]methyl]benzoic acid 449208-57-5P, 3-Benzyl-2.4-dioxo-1.2.3.4-
       tetrahydroquinazoline-6-carboxylic acid benzyl ester 449208-82-6P
       449209-00-1P, [4-[[6-(4-Methoxybenzylcarbamoyl)-1-methyl-2,4-dioxo-1,4-
       dihydro-2H-quinazolin-3-yl]methyl]phenyl]acetic acid 449209-16-9P.
       Methyl 3-[[6-(4-methoxybenzylcarbamoyl)-1-methyl-2,4-dioxo-1.4-dihydro-2H-
       quinazolin-3-yl]methyl]benzoate 449209-18-1P, (E)-Methyl
       4-[6-(4-methoxybenzylcarbamoyl)-1-methyl-2,4-dioxo-1,4-dihydro-2H-
       quinazolin-3-yl]but-2-enoate 449209-20-5P, Methyl 5-[[6-(4-
       methoxybenzylcarbamoyl)-1-methyl-2,4-dioxo-1,4-dihydro-2H-quinazolin-3-
       yl]methyl]furan-2-carboxylate 449209-22-7P. Methyl 5-[[6-(4-
       methoxybenzylcarbamoyl)-1-methyl-2,4-dioxo-1,4-dihydro-2H-quinazolin-3-
       yl]methyl]thiophene-2-carboxylate 449209-24-9P 449209-37-4P. Methyl
       2-chloro-4-[[6-(4-methoxybenzylcarbamoyl)-1-methyl-2,4-dioxo-1,4-dihydro-
       2H-quinazolin-3-yl]methyl]benzoate 449209-43-2P, Methyl
       2-methoxy-4-[[6-(4-methoxybenzylcarbamoyl)-1-methyl-2.4-dioxo-1.4-dihydro-
       2H-quinazolin-3-yl]methyl]benzoate 449209-44-3P, 2-Methoxy-4-[[6-(4-
       methoxybenzylcarbamoyl)-1-methyl-2,4-dioxo-1,4-dihydro-2H-quinazolin-3-
       yl]methyl]benzoic acid 449209-45-4P, Methyl 2-hydroxy-4-[[6-(4-
       methoxybenzylcarbamoyl)-1-methyl-2,4-dioxo-1,4-dihydro-2H-quinazolin-3-
       yl]methyl]benzoate 449209-47-6P, Methyl 2-methyl-4-[[6-(4-
       \verb|methoxybenzy| carbamoy|)-1-methy|-2.4-dioxo-1.4-dihydro-2H-quinazo||in-3-dihydro-2H-quinazo|||in-3-dihydro-2H-quinazo|||-3-dihydro-2H-quinazo|||-3-dihydro-2H-quinazo|||-3-dihydro-2H-quinazo|||-3-dihydro-2H-quinazo|||-3-dihydro-2H-quinazo|||-3-dihydro-2H-quinazo|||-3-dihydro-2H-quinazo|||-3-dihydro-2H-quinazo|||-3-dihydro-2H-quinazo|||-3-dihydro-2H-quinazo|||-3-dihydro-2H-quinazo|||-3-dihydro-2H-quinazo|||-3-dihydro-2H-quinazo|||-3-dihydro-2H-quinazo|||-3-dihydro-2H-quinazo|||-3-dihydro-2H-quinazo|||-3-dihydro-2H-quinazo|||-3-dihydro-2H-quinazo|||-3-dihydro-2H-quinazo|||-3-dihydro-2H-quinazo|||-3-dihydro-2H-quinazo|||-3-dihydro-2H-quinazo|||-3-dihydro-2H-quinazo|||-3-dihydro-2H-quinazo|||-3-dihydro-2H-quinazo|||-3-dihydro-2H-quinazo|||-3-dihydro-2H-quinazo|||-3-dihydro-2H-quinazo|||-3-dihydro-2H-quinazo|||-3-dihydro-2H-quinazo|||-3-dihydro-2H-quinazo|||-3-dihydro-2H-quinazo|||-3-dihydro-2H-quinazo|||-3-dihydro-2H-quinazo|||-3-dihydro-2H-quinazo|||-3-dihydro-2H-quinazo|||-3-dihydro-2H-quinazo|||-3-dihydro-2H-quinazo|||-3-dihydro-2H-quinazo|||-3-dihydro-2H-quinazo|||-3-dihydro-2H-quinazo|||-3-dihydro-2H-quinazo|||-3-dihydro-2H-quinazo|||-3-dihydro-2H-quinazo|||-3-dihydro-2H-quinazo|||-3-dihydro-2H-quinazo|||-3-dihydro-2H-quinazo|||-3-dihydro-2H-quinazo|||-3-dihydro-2H-quinazo|||-3-dihydro-2H-quinazo|||-3-dihydro-2H-quinazo|||-3-dihydro-2H-quinazo|||-3-dihydro-2H-quinazo|||-3-dihydro-2H-quinazo|||-3-dihydro-2H-quinazo|||-3-dihydro-2H-quinazo|||-3-dihydro-2H-quinazo|||-3-dihydro-2H-quinazo|||-3-dihydro-2H-quinazo|||-3-dihydro-2H-quinazo|||-3-dihydro-2H-quinazo|||-3-dihydro-2H-quinazo|||-3-dihydro-2H-quinazo|||-3-dihydro-2H-quinazo|||-3-dihydro-2H-quinazo|||-3-dihydro-2H-quinazo|||-3-dihydro-2H-quinazo|||-3-dihydro-2H-quinazo|||-3-dihydro-2H-quinazo|||-3-dihydro-2H-quinazo|||-3-dihydro-2H-quinazo|||-3-dihydro-2H-quinazo|||-3-dihydro-2H-quinazo|||-3-dihydro-2H-quinazo|||-3-dihydro-2H-quinazo|||-3-dihydro-2H-quinazo|||-3-dihydro-2H-quinazo|||-3-dihydro-2H-quinazo|||-3-dihydro-2H-quinazo||||-3-dihydro-2H-quinazo||||
       vllmethyllbenzoate 449209-49-8P 449209-52-3P 449209-54-5P. Methyl
       4-[[6-(3-methoxybenzylcarbamoyl)-1-methyl-2,4-dioxo-1,4-dihydro-2H-
       quinazolin-3-yl]methyl]benzoate 449209-60-3P. 4-[[1-Methyl-6-((4-
       (methylsulfanyl)benzyl)carbamoyl)-2.4-dioxo-1.4-dihydro-2H-quinazolin-3-
       yl]methyl]benzoic acid methyl ester 449209-70-5P, 3-(4-Methoxybenzyl)-1-
       methyl-2.4-dioxo-1.2.3.4-tetrahydroguinazoline-6-carboxylic acid
       ((pyridin-4-yl)methyl)amide 449209-75-0P, Methyl 4-[[1-methyl-2.4-dioxo-
       6-[(pyridin-4-ylmethyl)carbamoyl]-1.4-dihydro-2H-quinazolin-3-
       yl]methyl]benzoate 449209-89-6P 449209-90-9P 449209-91-0P
       449209-95-4P 449209-98-7P, [5-[[6-(4-(Methoxy)benzylcarbamoyl)-1-methyl-
       2,4-dioxo-1,4-dihydro-2H-quinazolin-3-yl]methyl]pyridin-2-yl]carbamic acid
       tert-butyl ester 449210-36-0P, 4'-[[6-((4-Methoxybenzyl)carbamoyl)-1-
       methyl-2.4-dioxo-1,4-dihydro-2H-quinazolin-3-yl]methyl]biphenyl-2-
       carboxylic acid methyl ester 449210-88-2P, tert-Butyl
       1-[4-[[6-(4-methoxybenzylcarbamoyl)-1-methyl-2.4-dioxo-1.4-dihydro-2H-
       quinazolin-3-yl]methyl]phenyl]cyclopropanecarboxylate 449210-90-6P.
```

Page 12

```
3-Benzyl-6-benzylsulfanyl-1-methyl-1H-quinazoline-2.4-dione
 449210-98-4P. 4-[[6-(4-Methoxybenzylcarbamoyl)-1-methyl-2,4-dioxo-1.4-
 dihydro-2H-quinazoline-3-yl]methyl]benzoic acid chloromethyl ester
 449210-99-5P 449211-01-2P 474663-15-5P, Ethyl 2-Fluoro-4-[[6-(4-
 methoxybenzylcarbamoyl)-1-methyl-2.4-dioxo-1.4-dihydro-2H-quinazolin-3-
 yl]methyl]benzoate
 RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic
 preparation); THU (Therapeutic use); BIOL (Biological study); PREP
 (Preparation): RACT (Reactant or reagent): USES (Uses)
    (MMP13 inhibitor; preparation of quinazolines as specific inhibitors of
    type-13 matrix metalloprotease)
449208-01-9P, 3-Benzyl-2.4-dioxo-1.2,3,4-tetrahydroquinazoline-6-
 carboxylic acid benzylamide 449208-03-1P, 3-Benzyl-2,4-dioxo-1,2,3,4-
 tetrahydroguinazoline-6-carboxylic acid (benzo[1,3]dioxol-5-ylmethyl)amide
 449208-04-2P, 3-Benzyl-2.4-dioxo-1,2.3.4-tetrahydroquinazoline-6-
 carboxylic acid (2-thienylmethyl)amide 449208-06-4P.
 3-Benzyl-2,4-dioxo-1,2,3,4-tetrahydroquinazoline-6-carboxylic acid
 (3-pyridylmethyl)amide 449208-07-5P 449208-08-6P 449208-09-7P
 449208-10-0P, 3-Benzyl-1-methyl-2,4-dioxo-1,2,3,4-tetrahydroquinazoline-6-
 carboxylic acid (benzo[1.3]dioxol-5-ylmethyl)amide 449208-11-1P.
 3-Benzyl-1-methyl-2,4-dioxo-1,2,3,4-tetrahydroquinazoline-6-carboxylic
 acid benzylamide 449208-12-2P, Methyl 4-[[[1-(3-benzyl-1-methyl-2.4-
 dioxo-1,2,3,4-tetrahydroquinazolin-6-yl)methanoyl]amino]methyl]benzoate
 449208-13-3P, 3-Benzyl-1-methyl-2,4-dioxo-1,2,3,4-tetrahydroquinazoline-6-
 carboxylic acid [4-hydroxy-3-methoxybenzyl]amide 449208-15-5P.
 3-Benzyl-1-methyl-2,4-dioxo-1,2,3,4-tetrahydroquinazoline-6-carboxylic
 acid (4-pyridylmethyl)amide 449208-16-6P, 1-Methyl-2,4-dioxo-3-phenethyl-
 1,2,3,4-tetrahydroquinazoline-6-carboxylic acid [benzo[1,3]dioxol-5-
 ylmethyl]amide 449208-20-2P, 3-(4-Methoxybenzyl)-2.4-dioxo-1.2,3.4-
 tetrahydroguinazoline-6-carboxylic acid [benzo[1,3]dioxol-5-ylmethyl]amide
 449208-22-4P, 3-(4-Methoxybenzyl)-1-methyl-2,4-dioxo-1,2,3,4-
 tetrahydroquinazoline-6-carboxylic acid [benzo[1.3]dioxol-5-ylmethyl]amide
               449208-25-7P, 3-(1-(Naphth-1-yl)ethyl)-2,4-dioxo-1,2,3,4-
 449208-23-5P
 tetrahydroquinazoline-6-carboxylic acid [benzo[1.3]dioxol-5-ylmethyl]amide
 449208-26-8P, 2,4-Dioxo-3-((pyridin-4-y1)methyl)-1,2,3,4-
 tetrahydroquinazoline-6-carboxylic acid [benzo[1,3]dioxol-5-ylmethyl]amide
 449208-32-6P. 2.4-Dioxo-3-(thien-2-ylmethyl)-1,2,3,4-tetrahydroquinazoline-
 6-carboxylic acid benzylamide 449208-36-0P, 1-Methyl-2,4-dioxo-3-(thien-
 2-ylmethyl)-1,2,3,4-tetrahydroquinazoline-6-carboxylic acid benzylamide
 449208-37-1P, 2,4-Dioxo-3-(thien-2-ylmethyl)-1,2,3,4-tetrahydroquinazoline-
 6-carboxylic acid [benzo[1,3]dioxol-5-ylmethyl]amide 449208-38-2P.
 1-Methyl-2,4-dioxo-3-(thien-2-ylmethyl)-1,2,3,4-tetrahydroquinazoline-6-
 carboxylic acid [benzo[1,3]dioxol-5-ylmethyl]amide 449208-39-3P.
 3-(4-Chlorobenzyl)-2,4-dioxo-1,2,3,4-tetrahydroquinazoline-6-carboxylic
 acid [benzo[1,3]dioxol-5-ylmethyl]amide 449208-40-6P.
 3-(4-Chlorobenzyl)-1-methyl-2,4-dioxo-1,2,3,4-tetrahydroquinazoline-6-
 carboxylic acid [benzo[1.3]dioxol-5-ylmethyl]amide 449208-41-7P.
 1,3-Dimethyl-2,4-dioxo-1,2,3,4-tetrahydroquinazoline-6-carboxylic acid
 [benzo[1,3]dioxol-5-ylmethyl]amide 449208-42-8P, 3-((Benzo[1,3]dioxol-5-
 yl)methyl)-2.4-dioxo-1.2.3.4-tetrahydroquinazoline-6-carboxylic acid
 [benzo[1.3]dioxol-5-ylmethyl]amide 449208-46-2P, 3-((Benzo[1.3]dioxol-5-
 yl)methyl)-1-methyl-2.4-dioxo-1.2.3.4-tetrahydroquinazoline-6-carboxylic
 acid [benzo[1,3]dioxol-5-ylmethyl]amide 449208-47-3P.
 3-Benzyl-1-ethyl-2,4-dioxo-1,2,3,4-tetrahydroquinazoline-6-carboxylic acid
 [benzo[1.3]dioxol-5-ylmethyl]amide 449208-48-4P. 3-Benzyl-1-
 cyclopropylmethyl-2,4-dioxo-1,2,3,4-tetrahydroquinazoline-6-carboxylic
 acid [benzo[1.3]dioxol-5-ylmethyl]amide 449208-49-5P.
 3-Benzyl-1-isobutyl-2.4-dioxo-1.2.3.4-tetrahydroquinazoline-6-carboxylic
 acid [benzo[1,3]dioxol-5-ylmethyl]amide 449208-56-4P.
 1-Methyl-2.4-dioxo-3-((E)-3-phenylpropenyl)-1.2.3.4-tetrahydroquinazoline-
 6-carboxylic acid [benzo[1.3]dioxol-5-ylmethyl]amide 449208-58-6P.
 \hbox{$3-$Benzyl-1-methyl-2.4-dioxo-1.2.3,4-tetrahydroquinazoline-6-carboxylic}
 acid benzyl ester 449208-59-7P, 3-Benzyl-2,4-dioxo-1,2,3,4-
 tetrahydroquinazoline-6-carboxylic acid 4-pyridylmethyl ester
```

Truong 10/075954 Page 13

449208-60-0P 449208-61-1P. 3-Benzyl-2.4-dioxo-1.2.3.4tetrahydroguinazoline-6-carboxylic acid [Benzo[1.3]dioxol-5-yl]methyl 449208-62-2P. 3-Benzyl-1-methyl-2.4-dioxo-1.2.3.4ester tetrahydroquinazoline-6-carboxylic acid [Benzo[1.3]dioxol-5-yl]methyl 449208-63-3P. 1-Benzyl-2.4-dioxo-3-((pyridin-4-yl)methyl)-1.2.3.4tetrahydroquinazoline-6-carboxylic acid benzyl ester 449208-64-4P. 2,4-Dioxo-3-(thien-2-ylmethyl)-1,2,3,4-tetrahydroquinazoline-6-carboxylic acid 4-Pyridylmethyl ester 449208-65-5P, 3-((Benzo[1.3]dioxol-5y1)methy1)-2.4-dioxo-1.2.3.4-tetrahydroquinazoline-6-carboxylic acid 4-Pyridylmethyl ester 449208-66-6P. Benzyl 3-benzyl-2.4-dioxo-1.2.3.4tetrahydropyrido[2.3-d]pyrimidine-6-carboxylate 449208-67-7P. 3-Benzyl-6-methyl-1H-pyrido[2,3-d]pyrimidine-2,4-dione 449208-69-9P. 4-Pyridylmethyl 3-benzyl-2.4-dioxo-1.2.3.4-tetrahydropyrido[2.3d]pyrimidine-6-carboxylate 449208-70-2P. 3-Benzyl-4-oxo-2-thioxo-1.2.3.4tetrahydroquinazoline-6-carboxylic acid [benzo[1,3]dioxol-5-ylmethyl]amide 449208-71-3P, 4-[[6-(4-Hydroxybenzylcarbamoyl)-1-methyl-2,4-dioxo-1,4dihydro-2H-quinazolin-3-yl]methyl]benzoic acid 449208-72-4P 449208-77-9P 449208-73-5P 449208-74-6P 449208-75-7P 449208-76-8P 449208-79-1P 449208-80-4P 449208-81-5P 449208-83-7P 449208-78-0P 449208-89-3P 449208-84-8P 449208-85-9P 449208-87-1P 449208-88-2P 449208-93-9P, Ethyl 449208-91-7P 449208-92-8P 449208-90-6P [6-(4-methoxybenzylcarbamoyl)-1-methyl-2,4-dioxo-1,4-dihydro-2H-quinazolin-3-y1]acetate 449208-94-0P 449208-95-1P, Methyl 3-[6-(4methoxybenzylcarbamoyl)-1-methyl-2,4-dioxo-1,4-dihydro-2H-quinazolin-3vl]propionate 449208-96-2P, 3-[6-(4-Methoxybenzylcarbamoyl)-1-methyl-2.4dioxo-1,4-dihydro-2H-quinazolin-3-yl]propionic acid 449208-97-3P 449208-98-4P. 4-[6-(4-Methoxybenzylcarbamoyl)-1-methyl-2,4-dioxo-1,4dihydro-2H-quinazolin-3-yl]butyric acid 449208-99-5P. Methyl [4-[[6-(4-methoxybenzylcarbamoyl)-1-methyl-2.4-dioxo-1.4-dihydro-2Hquinazolin-3-yl]methyl]phenyl]acetate 449209-01-2P 449209-02-3P 449209-04-5P 449209-06-7P 449209-07-8P 449209-09-0P 449209-13-6P 449209-17-0P, 3-[[6-(4-Methoxybenzylcarbamoyl)-1-methyl-2.4-449209-14-7P dioxo-1,4-dihydro-2H-quinazolin-3-yl]methyl]benzoic acid 449209-19-2P. 4-[6-(4-Methoxybenzylcarbamoyl)-1-methyl-2,4-dioxo-1,4-dihydro-2Hquinazolin-3-yl]but-2-enoic acid 449209-21-6P, 5-[[6-(4-Methoxybenzylcarbamoyl)-1-methyl-2,4-dioxo-1,4-dihydro-2H-quinazolin-3yl]methyl]furan-2-carboxylic acid 449209-23-8P, 5-[[6-(4-Methoxybenzylcarbamoyl)-1-methyl-2.4-dioxo-1.4-dihydro-2H-quinazolin-3yl]methyl]thiophene-2-carboxylic acid 449209-25-0P 449209-26-1P 449209-29-4P 449209-30-7P 449209-31-8P 449209-27-2P 449209-28-3P 449209-34-1P 449209-36-3P 449209-39-6P. 449209-32-9P 449209-33-0P 2-Chloro-4-[[6-(4-methoxybenzylcarbamoyl)-1-methyl-2,4-dioxo-1,4-dihydro-2H-quinazolin-3-yl]methyl]benzoic acid 449209-40-9P 449209-41-0P 449209-46-5P. 2-Hydroxy-4-[[6-(4-methoxybenzylcarbamoyl)-1-methyl-2.4dioxo-1.4-dihydro-2H-quinazolin-3-yl]methyl]benzoic acid 449209-48-7P. 2-Methyl-4-[[6-(4-methoxybenzylcarbamoyl)-1-methyl-2,4-dioxo-1,4-dihydro-2H-quinazolin-3-yl]methyl]benzoic acid 449209-53-4P 449209-59-0P. 4-[[6-(3-Methoxybenzylcarbamoyl)-1-methyl-2.4-dioxo-1.4-dihydro-2Hquinazolin-3-yl]methyl]benzoic acid 449209-61-4P. 4-[[1-Methyl-6-(4methylsulfanylbenzylcarbamoyl)-2,4-dioxo-1,4-dihydro-2H-quinazolin-3yl]methyl]benzoic acid 449209-62-5P, 4-[[1-Methyl-2,4-dioxo-6-(4-yl]methyl]benzoic acid methyl ester 449209-63-6P. Methyl 4-[[6-(4-fluorobenzy]carbamoy])-1-methyl-2,4-dioxo-1,4-dihydro-2Hquinazolin-3-yl]methyl]benzoate 449209-64-7P, 4-[[6-(4-Fluorobenzylcarbamoyl)-1-methyl-2,4-dioxo-1,4-dihydro-2H-quinazolin-3yl]methyl]benzoic acid 449209-65-8P. Methyl 4-[[6-[(benzofurazan-5ylmethyl)carbamoyl]-1-methyl-2.4-dioxo-1.4-dihydro-2H-quinazolin-3y1]methy1]benzoate 449209-66-9P, 4-[[6-[(Benzofurazan-5ylmethyl)carbamoyl]-1-methyl-2.4-dioxo-1.4-dihydro-2H-quinazolin-3yl]methyl]benzoic acid 449209-67-0P. Methyl 4-[[6-(4-methoxybenzylcarbamoyl)-2,4-dioxo-1,4-dihydro-2H-quinazolin-3y1]methy1]benzoate 449209-68-1P. Methy1 4-[[1-ethy1-6-(4methoxybenzylcarbamoyl)-2.4-dioxo-1.4-dihydro-2H-quinazolin-3-

```
yl]methyl]benzoate 449209-69-2P. 4-[[1-Ethyl-6-(4-
methoxybenzylcarbamoyl)-2,4-dioxo-1,4-dihydro-2H-quinazolin-3-
yl]methyl]benzoic acid 449209-71-6P, 3-(4-Hydroxybenzyl)-1-methyl-2.4-
dioxo-1.2.3.4-tetrahydroquinazoline-6-carboxylic acid ((pyridin-4-
yl)methyl)amide 449209-72-7P, 3-(4-Cyanobenzyl)-1-methyl-2,4-dioxo-
1.2.3.4-tetrahydroquinazoline-6-carboxylic acid ((pyridin-4-
yl)methyl)amide 449209-74-9P, 1-Methyl-2,4-dioxo-3-(3-(pyridin-4-
yl)propenyl)-1.2.3.4-tetrahydroquinazoline-6-carboxylic acid
((pyridin-4-yl)methyl)amide 449209-76-1P, 4-[[1-Methyl-2.4-dioxo-6-
[(pyridin-4-ylmethyl)carbamoyl]-1.4-dihydro-2H-quinazolin-3-
yl]methyl]benzoic acid hydrochloride 449209-77-2P, Methyl
[4-[[1-methy]-2,4-dioxo-6-[(pyridin-4-ylmethyl)carbamoyl]-1,4-dihydro-2H-
quinazolin-3-yl]methyl]phenyl]acetate 449209-78-3P, [4-[[1-Methyl-2,4-
dioxo-6-[(pyridin-4-ylmethyl)carbamoyl]-1,4-dihydro-2H-quinazolin-3-
yl]methyl]phenyl]acetic acid hydrochloride 449209-79-4P 449209-80-7P
449209-81-8P, Methyl [6-[(1,3-Benzodioxol-5-ylmethyl)carbamoyl]-3-benzyl-
2,4-dioxo-1,4-dihydro-2H-quinazolin-1-yl]acetate 449209-82-9P.
[6-[(1,3-Benzodioxol-5-ylmethyl)carbamoyl]-3-benzyl-2,4-dioxo-3.4-dihydro-
2H-quinazolin-1-yl]acetic acid 449209-83-0P, Methyl 4-[[6-[(1,3-
benzodioxol-5-ylmethyl)carbamoyl]-1-methyl-2.4-dioxo-1.4-dihydro-2H-
quinazolin-3-yl]methyl]benzoate 449209-84-1P, 4-[[6-[(1.3-Benzodioxol-5-
ylmethyl)carbamoyl]-1-methyl-2,4-dioxo-1,4-dihydro-2H-quinazolin-3-
yl]methyl]benzoic acid 449209-85-2P, 3-Benzyl-1-methyl-2.4-dioxo-1.2.3.4-
tetrahydroquinazoline-6-carboxylic acid (4-(sulfamoyl)benzyl)amide
449209-86-3P. 3-Benzyl-1-methyl-2.4-dioxo-1.2.3.4-tetrahydroquinazoline-6-
carboxylic acid [3-(pyridin-4-ylsulfanyl)propyl]amide 449209-87-4P.
3-Benzyl-1-methyl-2,4-dioxo-1,2,3,4-tetrahydroquinazoline-6-carboxylic
acid (4-morpholin-4-ylbutyl)amide 449209-88-5P
                                                 449209-92-1P.
3-Benzyl-1-methyl-2.4-dioxo-1,2,3,4-tetrahydroquinazoline-6-carboxylic
acid (4-((dimethylcarbamoyl)methoxy)benzyl)amide 449209-93-2P
449209-94-3P 449209-96-5P. 3-Benzyl-1-methyl-2.4-dioxo-1.2.3.4-
tetrahydroquinazoline-6-carboxylic acid (4-(dimethylcarbamoyl)benzyl)amide
449209-97-6P 449209-99-8P 449210-00-8P, 1,3-Dimethyl-2,4-dioxo-1,2,3,4-
tetrahydropyrido[2,3-d]pyrimidine-6-carboxylic acid [benzo[1,3]dioxol-5-
ylmethyl]amide 449210-01-9P, 1.3-Dimethyl-2.4-dioxo-1.2.3.4-
tetrahydropyrido[3,4-d]pyrimidine-6-carboxylic acid [benzo[1,3]dioxol-5-
ylmethyl]amide 449210-03-1P, 3-Benzyl-1-methyl-2,4-dioxo-1,2,3,4-
tetrahydropyrido[2,3-d]pyrimidine-6-carboxylic acid [benzo[1,3]dioxol-5-
ylmethyl]amide 449210-07-5P, 4-[[6-(4-Methoxybenzylcarbamoyl)-1-methyl-
2,4-dioxo-1,4-dihydro-2H-pyrido[2,3-d]pyrimidin-3-yl]methyl]benzoic acid
449210-11-1P 449210-12-2P 449210-13-3P, 3-Benzyl-1-methyl-2,4-
dioxo-1,2,3,4-tetrahydropyrido[3,4-d]pyrimidine-6-carboxylic acid
[benzo[1,3]dioxol-5-ylmethyl]amide 449210-20-2P, Methyl
4-[[6-(4-Methoxybenzylcarbamoyl)-1-methyl-2,4-dioxo-1.4-dihydro-2H-
pyrido[3,4-d]pyrimidin-3-yl]methyl]benzoate 449210-23-5P.
tert-Butyl 4-[[6-(4-methoxybenzylcarbamoyl)-1-methyl-2.4-dioxo-1.4-dihydro-
2H-pyrido[3,4-d]pyrimidin-3-yl]methyl]benzoate 449210-24-6P.
4-[[6-(3-Methoxybenzylcarbamoyl)-1-methyl-2,4-dioxo-1,4-dihydro-2H-
pyrido[3.4-d]pyrimidin-3-yl]methyl]benzoic acid 449210-27-9P
449210-28-0P, 3-Benzyl-1-methyl-6-(3-phenylpropionyl)-1H-quinazoline-2.4-
dione 449210-29-1P 449210-30-4P
                                    449210-31-5P, 3-Benzyl-1-methyl-6-[2-
(pyridin-4-ylsulfanyl)acetyl]-1H-quinazoline-2,4-dione 449210-32-6P
449210-33-7P 449210-34-8P 449210-37-1P, 4'-[[6-(4-
Methoxybenzylcarbamoyl)-1-methyl-2,4-dioxo-1,4-dihydro-2H-quinazolin-3-
yl]methyl]biphenyl-2-carboxylic acid 449210-39-3P, 2-Fluoro-4-[[6-(4-
methoxybenzylcarbamoyl)-1-methyl-2,4-dioxo-1,4-dihydro-2H-quinazolin-3-
yl]methyl]benzoic acid 449210-40-6P, 2-Methoxy-4-[[6-(4-
methoxybenzylcarbamoyl)-1-methyl-2,4-dioxo-1,4-dihydro-2H-quinazolin-3-
yl]methyl]benzoic acid 2-dimethylaminoethyl ester 449210-41-7P.
4-[[6-(4-Methoxybenzylcarbamoyl)-1-methyl-2,4-dioxo-1,4-dihydro-2H-
quinazolin-3-yl]methyl]-2-methylbenzoic acid 2-dimethylaminoethyl ester
449210-42-8P 449210-43-9P. [4-[6-(4-Methoxybenzylcarbamoyl)-1-methyl-2.4-
dioxo-1.4-dihydro-2H-quinazolin-3-yl]phenyl]acetic acid
1-Methyl-3-(1-(naphthalen-1-yl)ethyl)-2.4-dioxo-1.2.3.4-
```

```
tetrahydroquinazoline-6-carboxylic acid [benzo[1,3]dioxol-5-ylmethyl]amide
449210-47-3P, 4-[[6-(4-Methoxybenzylcarbamoyl)-1-methyl-2,4-dioxo-
1.4-dihydro-2H-pyrido[3.4-d]pyrimidin-3-yl]methyl]benzoic acid
449210-49-5P, 3-(3-Fluorobenzyl)-1-methyl-2.4-dioxo-1.2.3.4-
tetrahydroquinazoline-6-carboxylic acid ((pyridin-4-yl)methyl)amide
449210-51-9P. 3-(3-Fluorobenzyl)-1-methyl-2,4-dioxo-1,2,3,4-
tetrahydroquinazoline-6-carboxylic acid ((2-methoxypyridin-4-
yl)methyl)amide 449210-52-0P, 3-(3-Fluorobenzyl)-1-methyl-2,4-dioxo-
1.2.3.4-tetrahydroquinazoline-6-carboxylic acid ((pyridin-3-
yl)methyl)amide 449210-53-1P 449210-54-2P 449210-55-3P.
1-Ethyl-3-(3-fluorobenzyl)-2.4-dioxo-1.2.3.4-tetrahydroquinazoline-6-
carboxylic acid ((pyridin-4-yl)methyl)amide 449210-56-4P.
1-Ethyl-3-(3-fluorobenzyl)-2.4-dioxo-1,2,3,4-tetrahydroquinazoline-6-
carboxylic acid ((pyridin-3-yl)methyl)amide 449210-57-5P 449210-61-1P.
3-(4-Bromobenzyl)-1-methyl-2,4-dioxo-1,2,3,4-tetrahydroquinazoline-6-
carboxylic acid ((2-methoxypyridin-4-yl)methyl)amide 449210-62-2P.
3-(3.4-Difluorobenzyl)-1-methyl-2.4-dioxo-1.2.3.4-tetrahydroquinazoline-6-
carboxylic acid (pyridin-3-ylmethyl)amide 449210-66-6P,
3-(3.4-Difluorobenzyl)-1-methyl-2,4-dioxo-1,2,3,4-tetrahydroquinazoline-6-
carboxylic acid (pyridin-4-ylmethyl)amide 449210-67-7P
                                                         449210-68-8P,
3-(3-Chloro-4-fluorobenzyl)-1-methyl-2,4-dioxo-1,2,3,4-
tetrahydroguinazoline-6-carboxylic acid ((pyridin-4-yl)methyl)amide
449210-72-4P 449210-73-5P 449210-74-6P 449210-75-7P 449210-76-8P.
3-(4-Chlorobenzyl)-1-methyl-2,4-dioxo-1,2,3,4-tetrahydroquinazoline-6-
carboxylic acid ((pyridin-4-yl)methyl)amide 449210-78-0P.
3-(4-Fluorobenzyl)-1-methyl-2,4-dioxo-1,2,3,4-tetrahydroquinazoline-6-
carboxylic acid ((pyridin-4-yl)methyl)amide 449210-79-1P.
3-(4-Fluorobenzyl)-1-methyl-2,4-dioxo-1,2,3,4-tetrahydroquinazoline-6-
carboxylic acid ((pyridin-3-yl)methyl)amide 449210-81-5P.
3-(4-Chlorobenzyl)-1-methyl-2,4-dioxo-1,2,3,4-tetrahydroquinazoline-6-
                                                           449210-84-8P
carboxylic acid ((pyridin-3-yl)methyl)amide 449210-82-6P
449210-85-9P, 3-(4-Fluorobenzyl)-1-methyl-2.4-dioxo-1,2,3,4-
tetrahydroquinazoline-6-carboxylic acid ((2-methoxypyridin-4-
yl)methyl)amide 449210-87-1P, 3-(4-Chlorobenzyl)-1-methyl-2,4-dioxo-
1,2,3,4-tetrahydroquinazoline-6-carboxylic acid ((2-methoxypyridin-4-
yl)methyl)amide 449210-89-3P, 1-[4-[[6-(4-Methoxybenzylcarbamoyl)-1-
methyl-2,4-dioxo-1,4-dihydro-2H-quinazolin-3-yl]methyl]phenyl]cyclopropane
carboxylic acid 449210-92-8P, 3-Benzyl-1-methyl-6-
((phenylmethyl)sulfinyl)-1H-quinazoline-2,4-dione 449210-93-9P,
3-Benzyl-1-methyl-6-((phenylmethyl)sulfonyl)-1H-quinazoline-2.4-dione
449210-94-0P 449210-95-1P. 4-[[6-(4-Methoxybenzylcarbamoyl)-1-methyl-2,4-
dioxo-1,4-dihydro-2H-quinazoline-3-yl]methyl]benzoic acid
3-(dimethylamino)-2,2-dimethylpropyl ester 449210-96-2P,
4-[[6-((4-Methoxybenzyl)carbamoyl)-1-methyl-2,4-dioxo-1,4-dihydro-2H-
quinazoline-3-vllmethyl]benzoic acid 2-(dimethylamino)-2-methylpropyl
      449210-97-3P, 4-[[6-(4-Methoxybenzylcarbamoyl)-1-methyl-2,4-dioxo-
1.4-dihydro-2H-quinazoline-3-yl]methyl]benzoic acid 2-dimethylaminoethyl
        449211-00-1P 449211-04-5P 449211-08-9P 449211-12-5P.
4-[[6-((3-Methoxybenzylcarbamoyl)methyl)-2,4-dioxo-1,4-dihydro-2H-
quinazolin-3-yl]methyl]benzoic acid methyl ester 449211-14-7P.
4-[[1-Ethyl-2.4-dioxo-6-((4-(trifluoromethoxy)benzyl)carbamoyl)-1,4-
dihydro-2H-quinazolin-3-yl]methyl]benzoic acid methyl ester
449211-16-9P. 4-[[1-Methyl-2.4-dioxo-6-[(pyridin-4-ylmethyl)carbamoyl]-1.4-
dihydro-2H-quinazolin-3-yl]methyl]benzoic acid 449211-18-1P.
[4-[[1-Methyl-2.4-dioxo-6-[(pyridin-4-ylmethyl)carbamoyl]-1.4-dihydro-2H-
quinazolin-3-yl]methyl]phenyl]acetic acid
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
(Uses)
   (MMP13 inhibitor; preparation of quinazolines as specific inhibitors of
   type-13 matrix metalloprotease)
                                     23965-06-2P, 3-Benzyl-6-bromo-1H-
4315-09-7P, 4-Nitroisophthalic acid
quinazoline-2,4-dione
                      33857-88-4P
                                     63746-12-3P, Dimethyl
4-aminoisophthalate 69048-70-0P, Dimethyl 4-nitroisophthalate
```

```
69209-73-0P 151979-21-4P, 5-Iodo-2-((methyl)amino)benzoic acid
177913-48-3P. Dimethyl 4-amino-1-hydroxycyclohexa-3,5-diene-1,3-
dicarboxylate 184681-83-2P, 1,3-Dimethyl-2,4-dioxo-1,2,3,4-
tetrahydropyrido[2,3-d]pyrimidine-6-carboxylic acid 209604-61-5P.
3-Benzyl-2.4-dioxo-1.2.3.4-tetrahydroquinazoline-6-carboxylic acid methyl
ester 221540-53-0P, 3-(4-Methoxybenzyl)-2.4-dioxo-1.2.3.4-
tetrahydroquinazoline-6-carboxylic acid methyl ester 342644-48-8P.
3-Benzyl-1-methyl-2.4-dioxo-1.2.3.4-tetrahydropyrido[2.3-d]pyrimidine-6-
carboxylic acid ethyl ester 449207-91-4P, 3-Benzyl-2.4-dioxo-1.2.3.4-
tetrahydroquinazoline-6-carboxylic acid 449207-92-5P 449207-93-6P.
3-Benzyl-2,4-dioxo-1,2,3,4-tetrahydroquinazoline-6-carbonitrile
449207-94-7P. 3-Benzyl-1-methyl-2,4-dioxo-1,2,3,4-tetrahydroquinazoline-6-
carboxylic acid 449207-95-8P, 3-Benzyl-1-methyl-2,4-dioxo-1,2,3,4-
tetrahydroguinazoline-6-carboxylic acid methyl ester 449207-96-9P.
1-Methyl-3-(3-fluorobenzyl)-2,4-dioxo-1,2,3,4-tetrahydroquinazoline-6-
carboxylic acid 449207-97-0P, 3-(3-Fluorobenzyl)-2.4-dioxo-1.2.3.4-
tetrahydroquinazoline-6-carboxylic acid methyl ester 449207-98-1P.
1-Methyl-3-(3-fluorobenzyl)-2.4-dioxo-1.2.3.4-tetrahydroquinazoline-6-
carboxylic acid methyl ester 449207-99-2P, 1-Ethyl-3-(3-fluorobenzyl)-
2,4-dioxo-1,2,3,4-tetrahydroquinazoline-6-carboxylic acid 449208-00-8P.
1-Ethyl-3-(3-fluorobenzyl)-2,4-dioxo-1,2,3,4-tetrahydroquinazoline-6-
carboxylic acid methyl ester 449208-17-7P. 2.4-Dioxo-3-phenethyl-1.2.3.4-
tetrahydroguinazoline-6-carboxylic acid methyl ester 449208-18-8P.
2.4-Dioxo-3-phenethyl-1.2.3.4-tetrahydroquinazoline-6-carboxylic acid
449208-19-9P, 2,4-Dioxo-3-phenethyl-1,2,3,4-tetrahydroquinazoline-6-
carboxylic acid [benzo[1,3]dioxol-5-ylmethyl]amide 449208-21-3P.
3-(4-Methoxybenzyl)-2,4-dioxo-1,2,3,4-tetrahydroquinazoline-6-carboxylic
acid 449208-24-6P, 3-(4-Methoxybenzyl)-2.4-dioxo-1.2.3.4-
tetrahydroguinazoline-6-carboxylic acid (4-methoxybenzyl)amide
449208-27-9P, Dimethyl 4-(N'-((pyridin-4-yl)methyl)ureido)isophthalate
449208-29-1P, 2,4-Dioxo-3-((pyridin-4-yl)methyl)-1,2,3,4-
tetrahydroquinazoline-6-carboxylic acid methyl ester 449208-31-5P.
2,4-Dioxo-3-((pyridin-4-yl)methyl)-1,2,3,4-tetrahydroquinazoline-6-
carboxylic acid 449208-33-7P 449208-34-8P, 2,4-Dioxo-3-(thien-2-
ylmethyl)-1,2,3,4-tetrahydroquinazoline-6-carboxylic acid methyl ester
449208-35-9P, 2,4-Dioxo-3-(thien-2-ylmethyl)-1,2,3,4-tetrahydroquinazoline-
6-carboxylic acid 449208-43-9P 449208-44-0P, 3-((Benzo[1,3]dioxol-5-
y1)methy1)-2.4-dioxo-1.2.3.4-tetrahydroquinazoline-6-carboxylic acid
methyl ester 449208-45-1P, 3-((Benzo[1,3]dioxol-5-yl)methyl)-2,4-dioxo-
1.2.3,4-tetrahydroquinazoline-6-carboxylic acid 449208-51-9P.
1-Methyl-2,4-dioxo-1,2,3,4-tetrahydroquinazoline-6-carboxylic acid methyl
      449208-53-1P 449208-68-8P, 3-Benzyl-2,4-dioxo-1,2,3,4-
tetrahydropyrido[2,3-d]pyrimidine-6-carboxylic acid 449209-10-3P.
3-(4-Chlorosulfonylbenzyl)-1-methyl-2,4-dioxo-1,2,3,4-
tetrahydroquinazoline-6-carboxylic acid methyl ester 449209-11-4P.
3-(4-Dimethylsulfamoylbenzyl)-1-methyl-2,4-dioxo-1,2,3,4-
tetrahydroquinazoline-6-carboxylic acid methyl ester 449209-12-5P.
3-(4-Dimethylsulfamoylbenzyl)-1-methyl-2,4-dioxo-1.2.3.4-
tetrahydroguinazoline-6-carboxylic acid 449209-15-8P.
1-Methyl-3-(4-methylsulfamoylbenzyl)-2.4-dioxo-1,2,3,4-
tetrahydroquinazoline-6-carboxylic acid methyl ester 449209-50-1P.
2.4-Dioxo-1-methyl-3-(pyridin-4-ylmethyl)-1,2,3,4-tetrahydroquinazoline-6-
carboxylic acid methyl ester 449209-51-2P, 2,4-Dioxo-1-methyl-3-
(pyridine-4-ylmethyl)-1,2,3,4-tetrahydroquinazoline-6-carboxylic acid
449209-55-6P, 3-(4-Methoxycarbonylbenzyl)-2.4-dioxo-1,2,3,4-
tetrahydroquinazoline-6-carboxylic acid benzyl ester 449209-57-8P.
3-(4-Methoxycarbonylbenzyl)-1-methyl-2,4-dioxo-1,2,3,4-
tetrahydroquinazoline-6-carboxylic acid benzyl ester
                                                      449209-58-9P.
3-(4-Methoxycarbonylbenzyl)-1-methyl-2,4-dioxo-1,2,3.4-
tetrahydroquinazoline-6-carboxylic acid 449209-73-8P.
1-Methyl-2.4-dioxo-1.2.3.4-tetrahydroquinazoline-6-carboxylic acid
(pyridin-4-ylmethyl)amide 449210-02-0P, 1.3-Dimethyl-2,4-dioxo-1,2,3,4-
tetrahydropyrido[3,4-d]pyrimidine-6-carboxylic acid 449210-04-2P
449210-05-3P 449210-06-4P. 3-Benzyl-1-methyl-2.4-dioxo-1.2.3.4-
```

Truong 10/075954

```
tetrahydropyrido[2,3-d]pyrimidine-6-carboxylic acid 449210-08-6P.
1-Methyl-2,4-dioxo-1,2,3,4-tetrahydropyrido[2,3-d]pyrimidine-6-carboxylic
acid 449210-09-7P 449210-10-0P, Methyl 4-[[6-(4-
Methoxybenzylcarbamoyl)-1-methyl-2,4-dioxo-1,4-dihydro-2H-pyrido[2,3-
d]pyrimidin-3-yl]methyl]benzoate 449210-14-4P. 1-Benzyl-2.6-dioxo-
1.2.3.6-tetrahydropyrimidine-4-carboxaldehyde 449210-15-5P
449210-16-6P 449210-17-7P 449210-18-8P, 3-Benzyl-1-methyl-2,4-dioxo-
1.2.3.4-tetrahydropyrido[3.4-d]pyrimidine-6-carboxylic acid methyl ester
449210-19-9P, 3-Benzyl-1-methyl-2,4-dioxo-1,2,3,4-tetrahydropyrido[3,4-
d]pyrimidine-6-carboxylic acid 449210-21-3P, 1-Methyl-2.4-dioxo-1.2.3.4-
tetrahydropyrido[3,4-d]pyrimidine-6-carboxylic acid 449210-22-4P
449210-25-7P 449210-26-8P, tert-Butyl 4-[[6-(3-
Methoxybenzylcarbamoyl)-1-methyl-2,4-dioxo-1,4-dihydro-2H-pyrido[3.4-
d]pyrimidin-3-yl]methyl]benzoate 449210-58-6P, 3-(4-Bromobenzyl)-2.4-
dioxo-1.2.3.4-tetrahydroguinazoline-6-carboxylic acid methyl ester
449210-59-7P. 1-Methyl-3-(4-bromobenzyl)-2,4-dioxo-1.2.3,4-
tetrahydroquinazoline-6-carboxylic acid methyl ester 449210-60-0P.
1-Methyl-3-(4-bromobenzyl)-2,4-dioxo-1,2,3,4-tetrahydroquinazoline-6-
carboxylic acid 449210-63-3P. 3-(3,4-Difluorobenzyl)-2,4-dioxo-1,2,3.4-
tetrahydroquinazoline-6-carboxylic acid methyl ester 449210-64-4P.
1-Methyl-3-(3.4-difluorobenzyl)-2.4-dioxo-1.2.3.4-tetrahydroquinazoline-6-
carboxylic acid methyl ester 449210-65-5P. 1-Methyl-3-(3.4-
difluorobenzyl)-2.4-dioxo-1,2.3.4-tetrahydroquinazoline-6-carboxylic acid
449210-69-9P. 3-(3-Chloro-4-fluorobenzyl)-2.4-dioxo-1.2.3.4-
tetrahydroquinazoline-6-carboxylic acid methyl ester 449210-70-2P.
1-Methyl-3-(3-chloro-4-fluorobenzyl)-2,4-dioxo-1,2,3,4-
tetrahydroguinazoline-6-carboxylic acid methyl ester 449210-71-3P.
1-Methyl-3-(3-chloro-4-fluorobenzyl)-2.4-dioxo-1.2.3.4-
tetrahydroquinazoline-6-carboxylic acid 449210-77-9P.
1-Methyl-2.4-dioxo-1.2.3.4-tetrahydroguinazoline-6-carboxylic acid
(pyridazin-4-ylmethyl)amide 449210-80-4P. 1-Methyl-2,4-dioxo-1.2.3.4-
tetrahydroquinazoline-6-carboxylic acid (pyridin-3-ylmethyl)amide
449210-83-7P 449210-86-0P, 1-Methyl-2,4-dioxo-1,2,3,4-
tetrahydroguinazoline-6-carboxylic acid ((2-methoxypyridin-4-
v1)methy1)amide 449210-91-7P. 3-Benzy1-6-iodo-1-methy1-1H-quinazoline-
2,4-dione
RL: RCT (Reactant): SPN (Synthetic preparation): PREP (Preparation): RACT
(Reactant or reagent)
   (intermediate; preparation of quinazolines as specific inhibitors of type-13
   matrix metalloprotease)
9001-12-1, MMP-1 9004-06-2, MMP-12 79955-99-0, MMP 3 141256-52-2.
MMP 7 146480-35-5, MMP-2 146480-36-6, MMP-9 161384-17-4, MMP-14
175449-82-8. MMP-13
RL: BSU (Biological study, unclassified); BIOL (Biological study)
   (preparation of quinazolines as specific inhibitors of type-13 matrix
   metalloprotease)
78-73-9. Choline bicarbonate 78-77-3. Isobutyl bromide 79-07-2.
2-Chloroacetamide 96-32-2, Methyl bromoacetate 96-33-3, Methyl
acrylate 100-11-8, 4-Nitrobenzyl bromide 100-44-7, Benzyl chloride.
reactions 100-46-9, Benzylamine, reactions 100-51-6, Benzyl alcohol,
reactions 104-84-7, 4-Methylbenzylamine 104-86-9, 4-Chlorobenzylamine
105-36-2. Ethyl bromoacetate 105-39-5. Ethyl 2-chloroacetate 106-95-6.
Allyl bromide, reactions 106-96-7. Prop-2-ynyl bromide 108-00-9.
N.N-Dimethylethylene diamine 108-01-0, 2-(Dimethylamino)ethanol
119-68-6. N-Methylanthranilic acid 138-39-6. 4-
(Aminomethyl)benzenesulfonamide 140-75-0, 4-Fluorobenzylamine
140-88-5, Ethyl acrylate 332-48-9, 2-(4-Fluorophenoxy)ethyl bromide
351-52-0, 4-Chloromethyl-2-fluoro-1-methoxybenzene 459-46-1 495-76-1,
Piperonyl alcohol 540-51-2, 2-Bromoethanol 586-95-8, 4-Pyridylcarbinol
593-71-5. Chloroiodomethane 622-78-6. Benzyl isothiocyanate 622-95-7.
4-Chlorobenzyl bromide 637-59-2. 3-Phenylpropyl bromide 870-63-3.
1-Bromo-3-methylbut-2-ene 874-89-5. 4-Hydroxymethylbenzonitrile
874-98-6. 3-(Bromomethyl)-1-methoxyphenyl 938-09-0, 2-Chloroethyl phenyl
sulfone 1117-71-1, Methyl 4-bromocrotonate 1129-28-8, Methyl
```

```
3-(bromomethyl)benzoate 1943-82-4, Phenethyl isocyanate 2144-37-8.
     Methyl 5-(chloromethyl)-2-furoate 2393-23-9, 4-Methoxybenzylamine
     2417-72-3. Methyl 4-(bromomethyl)benzoate 2550-36-9,
     (Bromomethyl)cyclohexane 2620-50-0. Piperonylamine 2969-81-5. Ethyl
     4-bromobutyrate 3113-72-2, 5-Methyl-2-nitrobenzoic acid 3173-56-6.
     Benzyl isocyanate 3277-89-2. Phenethylmagnesium bromide 3395-91-3.
    Methyl 3-bromopropanoate 3731-52-0. 3-(Aminomethyl)pyridine 3731-53-1. 4-Picolylamine 4070-48-8 4637-24-5 5071-96-5. 3-Methoxybenzylamine
     5586-89-0 5794-88-7, 2-Amino-5-bromobenzoic acid 6232-11-7, Methyl
     4-(aminomethyl)benzoate hydrochloride 6321-07-9, 4-Morpholin-4-
     ylbutylamine 6482-24-2, 1-Bromo-2-methoxyethane 7005-47-2,
     2-(Dimethylamino)-2-methylpropanol 7051-34-5. Cyclopropylmethyl bromide
     7149-10-2. 4-Hydroxy-3-methoxybenzylamine hydrochloride 7398-42-7.
     Methyl 4-(bromomethyl)phenylacetate 10406-25-4 13734-41-3
    17201-43-3, 4-(Bromomethyl)benzonitrile 18469-52-8, Methyl 4-aminomethyl benzoate 19059-68-8, 3-(Dimethylamino)-2,2-dimethylpropanol
     22059-22-9, N-Hydroxyacetamidine 22600-30-2, Methyl 5-amino-2-furan
     carboxylate 25589-18-8, 3-Benzyl-6-methyl-1H-pyrimidine-2,4-dione
     26146-77-0. (E)-Cinnamyl bromide 27757-85-3, 2-Thienylmethylamine
     28188-41-2, 3-(Bromomethyl)benzonitrile 30260-66-3, Dimethylhydrazine
    30280-44-5, 4-Chlorobenzyl isocyanate 32863-31-3, 5-Bromomethylbenzofurazan 39077-96-8 40724-47-8, 4-
    \label{lem:bound} Bromomethylbenzenesulfonamide & 41886-04-8, 3-Bromomethyl-1-methylpiperidine & 50541-93-0, 4-Amino-1-benzylpiperidine & 55401-97-3,\\
     2-(Bromomethyl)pyridine 56651-60-6, 4-Methoxybenzyl isocyanate
     69966-55-8, 3-(Bromomethyl)pyridine 72235-53-1, 3,4-Difluorobenzylamine
     72235-56-4, 3-Chloro-4-fluorobenzylamine 74733-27-0, Methyl
     4-bromomethyl-2-methoxybenzoate 74733-28-1, Methyl 4-bromomethyl-2-
     methyl benzoate 78358-86-8, 1-(2-Bromoethyl)pyrrole 78826-46-7.
     (tert-Butoxy)acetyl chloride 83171-39-5, 4-Methylthiobenzylamine
     85070-57-1, Methyl 4-(bromomethyl)-2-fluorobenzoate 85147-14-4
     88442-63-1. 1-(1-Naphthyl)ethyl isocyanate 89583-07-3.
     4-(2-Bromoethyl)morpholine 93919-56-3, 4-Trifluoromethoxybenzylamine
     99067-96-6, (4-(Dimethylamino)benzyl)isocyanate 102422-56-0,
     3-Fluorobenzyl isocyanate 108052-76-2, tert-Butyl 4-bromomethylbenzoate
     108499-32-7, Methyl 5-bromomethylthiophene-2-carboxylate 114772-38-2
     114772-54-2, 2-(4-Bromomethylphenyl)benzonitrile 120788-70-7, Ethyl
     1,3-dimethy1-2,4-dioxo-1,2,3,4-tetrahydropyrido[2,3-d]pyrimidine-6-
     carboxylate 128674-45-3, 4-(3-Chloropropenyl)pyridine hydrochloride
                   138895-24-6, 6-Amino-3-benzyl-1H-pyrimidine-2,4-dione
     138402-33-2
     148900-69-0 154470-79-8, Methyl 1.3-dimethyl-2,4-dioxo-1,2.3.4-
     tetrahydropyrido[3.4-d]pyrimidine-6-carboxylate 155965-45-0
     220875-89-8, 5-(4-Chloromethylphenyl)-1-methyl-1H-tetrazole 221031-44-3.
     2-Chloro-1-(4-diethylaminophenyl)ethan-1-one 302912-23-8, 4-Bromobenzyl
     isocyanate 304873-96-9, tert-Butyl (5-bromomethylpyridin-2-yl)carbamate
     448965-87-5. tert-Butyl 1-(4-bromomethylphenyl)cyclopropanecarboxylate
     449208-54-2, 1-Methyl-2,4-dioxo-1,2,3,4-tetrahydroquinazoline-6-carboxylic
     acid 449209-03-4, 3-((E)-3-Chloropropenyl)pyridine 449209-05-6,
     4-((E)-3-Chloropropenyl)pyridine 449209-08-9, 3-(4-
     (Methanesulfonyl)benzyl)-1-methyl-2,4-dioxo-1,2,3,4-tetrahydroquinazoline-
     6-carboxylic acid 449209-35-2. 3-(4-Chloromethylphenyl)-5-
     methy1[1,2,4]oxadiazole 449209-38-5, Methyl 2-chloro-4-
     chloromethylbenzoate 449209-42-1, 5-(4-Chloromethylphenyl)-2-methyl-2H-
     tetrazole 449209-56-7
     RL: RCT (Reactant): RACT (Reactant or reagent)
        (reactant; preparation of quinazolines as specific inhibitors of type-13
        matrix metalloprotease)
RE.CNT 18
              THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD
(1) Abou-Hadeed, K: PTERIDINES 1996, V7(4), P113 HCAPLUS
(2) Anon; AMBINTER: EXPLORATORY LIBRARY 2002
(3) Anon: CHEMSTAR PRODUCT LIST 2001
```

RE

(4) Anon: SCIENTIFIC EXCHANGE PRODUCT LIST 2001

(5) Anon; SCREENING COLLECTION 2000

- (6) Bemis, G; WO 9964400 A 1999 HCAPLUS
- (7) Brittelli. D: WO 9743239 A 1997 HCAPLUS
- (8) Chen, J; JOURNAL OF THE AMERICAN CHEMICAL SOCIETY 2000, V122, P9648 HCAPLUS
- (9) Ciba Geigy Ag: DE 2441959 A 1975 HCAPLUS
- (10) Ghose. A; J MED CHEM 1984, V27(7), P901 HCAPLUS
- (11) Kim, Y: CHEMISTRY AND BIOLOGY OF PTERIDINES AND FOLATES 1997. PROCEEDINGS OF THE INTERNATIONAL SYMPOSIUM ON PTERIDINES AND FOLATES, 11TH 1997. P41 MEDLINE
- (12) Lespagnol. A: BULL SOC PHARM LILLE 1977, V33(1). P67 HCAPLUS
- (13) Liverton, N; BIOORGANIC & MEDICINAL CHEMISTRY LETTERS 1998, V8(5), P483 HCAPLUS
- (14) Murata, S; CHÉMISTRY AND BIOLOGY OF PTERIDINES AND FOLATES 1997, PROCEEDINGS OF THE INTERNATIONAL SYMPOSIUM ON PTERIDINES AND FOLATES, 11TH 1997, P17 HCAPLUS
- (15) Nesterov: SU 119879 A 1959 HCAPLUS
- (16) Ogawa, H; CHEM PHARM BULL 1988, V36(6), P2253 HCAPLUS
- (17) Reiter, L; BIOORGANIC & MEDICINAL CHEMISTRY LETTERS 1999, V9(2). P127 HCAPLUS
- (18) Sladowska, H: FARMACO, ED SCI 1986, V41(12), P954 HCAPLUS
- IT 449210-13-3P. 3-Benzyl-1-methyl-2.4-dioxo-1.2.3.4-tetrahydropyrido[3.4-d]pyrimidine-6-carboxylic acid [benzo[1.3]dioxol-5-ylmethyl]amide

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

RN 449210-13-3 HCAPLUS

CN Pyrido[3.4-d]pyrimidine-6-carboxamide. N-(1.3-benzodioxol-5-ylmethyl)1.2.3.4-tetrahydro-1-methyl-2.4-dioxo-3-(phenylmethyl)- (9CI) (CA INDEX

- L16 ANSWER 4 OF 4 HCAPLUS COPYRIGHT 2005 ACS on STN
- AN 2002:637472 HCAPLUS
- DN 137:201321
- ED Entered STN: 23 Aug 2002
- TI Preparation of substituted isophthalic acid derivatives, multicyclic pyrimidinediones and analogs thereof as matrix metalloproteinase inhibitors
- IN Andrianjara, Charles: Ortwine, Daniel Fred; Pavlovsky, Alexander Gregory; Roark, William Howard
- PA Warner-Lambert Company, USA
- SO PCT Int. Appl., 173 pp.

CODEN: PIXXD2

- DT Patent
- LA English
- IC ICM A61K
- CC 28-16 (Heterocyclic Compounds (More Than One Hetero Atom)) Section cross-reference(s): 1, 63

FAN.CNT 1

PATENT NO.		KIND	DATE	APPLICATION NO.	DATE	
•						
PΙ	WO 2002064080	A2	20020822	WO 2002-IB447	20020213	
	WO 2002064080	A3	20021212			

```
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
            CO. CR. CU. CZ. DE. DK. DM. DZ. EC. EE. ES. FI. GB. GD. GE. GH.
            GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
            LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
            PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
            UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU,
        RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH.
            CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,
            BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
    CA 2437643
                         AA 20020822 CA 2002-2437643
                                                                 20020213
                                         US 2002-75069
    US 2003078276
                               20030424
                                                                  20020213
                         A1
    EP 1361873
                         A2
                               20031119
                                         EP 2002-710275
                                                                 20020213
        R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
    BR 2002007864
                               20040309 BR 2002-7864
                                                                  20020213
                         Α
    JP 2004529874
                         T2
                               20040930
                                          JP 2002-563877
                                                                  20020213
    US 2005004126
                               20050106
                                           US 2004-835619
                                                                 20040429
                         A1
PRAI US 2001-268821P
                         Р
                               20010214
    US 2002-75069
                               20020213
                         В3
    WO 2002-IB447
                         W
                               20020213
CLASS
PATENT NO.
                CLASS PATENT FAMILY CLASSIFICATION CODES
                       _____
WO 2002064080
               TCM
                       A61K
                       4C022/CA02; 4C036/AD05; 4C036/AD12; 4C036/AD19;
JP 2004529874
               FTERM
                       4C036/AD27; 4C036/AD30; 4C050/AA01; 4C050/AA07;
                       4C050/BB06; 4C050/CC08; 4C050/EE04; 4C050/FF03;
                       4C050/GG03: 4C050/HH02: 4C055/AA01: 4C055/BB01;
                       4C055/CA01: 4C055/DA06: 4C055/DA17: 4C055/DB04:
                       4C055/DB08: 4C055/EA01: 4C063/AA01: 4C063/AA03:
                       4C063/BB08; 4C063/BB09; 4C063/CC31; 4C063/CC81;
                       4C063/CC92; 4C063/DD12; 4C063/DD31; 4C063/EE01;
                       4C065/AA04: 4C065/BB11: 4C065/CC01: 4C065/DD03:
                       4C065/EE03: 4C065/HH08: 4C065/JJ01: 4C065/LL04:
                       4C065/PP18: 4C071/AA01: 4C071/BB01: 4C071/CC21:
                       4C071/EE13; 4C071/FF05; 4C071/GG02; 4C071/HH08;
                       4C071/HH28; 4C071/JJ01; 4C071/LL01; 4C072/AA01;
                       4C072/BB02; 4C072/CC02; 4C072/CC16; 4C072/EE12;
                       4C072/FF09: 4C072/GG07: 4C072/GG09: 4C072/HH02:
                       4C072/UU01: 4C086/AA01: 4C086/AA02: 4C086/AA03:
                       4C086/BA13: 4C086/BC17: 4C086/BC46: 4C086/BC87:
                       4C086/CB05: 4C086/CB09: 4C086/CB26: 4C086/GA04:
                       4C086/GA07; 4C086/GA08; 4C086/GA10; 4C086/MA01;
                       4C086/MA04; 4C086/NA14; 4C086/ZA02; 4C086/ZA36;
                       4C086/ZA45: 4C086/ZA59: 4C086/ZA67: 4C086/ZA89:
                       4C086/ZA96: 4C086/ZA97: 4C086/ZB11: 4C086/ZB15:
                       4C086/ZB26: 4H006/AA01: 4H006/AA03: 4H006/AB20:
                       4H006/AB22; 4H006/AB23; 4H006/AB25; 4H006/AB27;
                       4H006/AB28; 4H006/BJ50; 4H006/BM30; 4H006/BM71;
                       4H006/BM72: 4H006/BP30: 4H006/BR30: 4H006/BT32:
                       4H006/BU26; 4H006/BV72; 4H006/KC30
                       A61K031/00: C07D213/30D2; C07D213/40B; C07D239/96;
US 2005004126
                ECLA
                       CO7D285/14D; CO7D285/24; CO7D317/54; CO7D317/58;
                       C07D401/06+239+211; C07D401/06+239+213;
                       C07D401/12+239+213: C07D405/12+317+213:
                       C07D405/12+317+239; C07D405/14+317+239+213;
                       C07D405/14+317+317+239; C07D409/06+333B+239;
                       C07D409/12+333B+239; C07D409/14+333B+239+213:
                       C07D409/14+333B+317+239: C07D471/04+239B+221B:
                       C07D487/04+235C+239C: C07D487/04+249C+239C:
                       C07D495/04+333B+239B; C07D513/04+277C+239C
```

- Title compds., I [R1 and R2 together may form a substituted aromatic ring or a heterocyclic ring; or R2 and R3 together may form substituted heterocycle; or R1, R3, or R4 = alkyl, arylalkyl, etc.; X = C. S: Y = O, N with provision when Y = N it forms a 5-membered heterocycle with R3] and II [R5, R6 = arylalkylamine, heterocyclylalkoxy, etc.; R7 = H. MeO, NO2, etc.]. are prepared and disclosed as matrix metalloproteinase (MMP) inhibitors. Thus, III was prepared in five steps via cyclocondensation of diethylmalonate and benzylurea with subsequent chlorination, substitution with hydrosulfide hydrate to form an in situ intermediate that was reacted with bromoacetaldehyde dimethylacetal, followed by acid catalyzed cyclization and substitution with benzylchloroformate. III was demonstrated to inhibit MMP13 with an IC50 value (in .mu.M) of 0.0230. I and II bind allosterically to the catalytic domain of MMP-13 and comprise a hydrophobic group, first and second hydrogen bond acceptors and at least $% \left(1\right) =\left(1\right) \left(1\right)$ one, and preferably both, of a third hydrogen bond acceptor and a second hydrophobic group. Cartesian coordinates for centroids of the above features are defined in the specification. When the ligand binds to MMP-13, the first, second and third (when present) hydrogen bond acceptors bond resp. with Thr245. Thr247 and Met 253, the first hydrophobic group locates within the S1' channel of MMP-13 and the second hydrophobic group (when present) is relatively open to solvent. The compds. specifically inhibit the matrix metalloproteinase-13 enzyme and thus are useful for treating diseases resulting from tissue breakdown, such as heart disease. multiple sclerosis, arthritis, atherosclerosis, and osteoporosis.
- ST pyrimidinedione prepn matrix metalloproteinase inhibitor; isophthalic carboxylate prepn matrix metalloproteinase inhibitor; metalloproteinase inhibitor pyrimidinedione antiinflammatory
- IT Antiarteriosclerotics

(antiatherosclerotics: preparation and pharmaceutical activity of substituted isophthalic acid derivs.. multicyclic pyrimidinediones and analogs thereof as matrix metalloproteinase inhibitors)

IT Lung, disease

(chronic obstructive: preparation and pharmaceutical activity of substituted isophthalic acid derivs., multicyclic pyrimidinediones and analogs thereof as matrix metalloproteinase inhibitors)

IT Heart, disease

(failure: preparation and pharmaceutical activity of substituted isophthalic acid derivs., multicyclic pyrimidinediones and analogs thereof as matrix metalloproteinase inhibitors)

IT Intestine, disease

(inflammatory; preparation and pharmaceutical activity of substituted isophthalic acid derivs., multicyclic pyrimidinediones and analogs thereof as matrix metalloproteinase inhibitors)

IT Combinatorial library

(isopthalic acid derivs.; combinatorial preparation and pharmaceutical

Truong 10/075954

Page 22

activity of substituted isophthalic acid derivs. as matrix metalloproteinase inhibitors) Eye. disease (macula, senile degeneration: preparation and pharmaceutical activity of substituted isophthalic acid derivs., multicyclic pyrimidinediones and analogs thereof as matrix metalloproteinase inhibitors) Anti-inflammatory agents Antiarthritics Antiasthmatics Antirheumatic agents Antitumor agents Arthritis **Asthma** Atherosclerosis Cardiovascular agents Human Multiple sclerosis Neoplasm 8 1 Osteoarthritis Osteoporosis Periodontium, disease Psoriasis Rheumatoid arthritis (preparation and pharmaceutical activity of substituted isophthalic acid derivs., multicyclic pyrimidinediones and analogs thereof as matrix metalloproteinase inhibitors) Multiple sclerosis Osteoporosis (therapeutic agents; preparation and pharmaceutical activity of substituted isophthalic acid derivs.. multicyclic pyrimidinediones and analogs thereof as matrix metalloproteinase inhibitors) 449790-74-3P 449790-84-5P 449790-90-3P 449791-35-9P RL: CPN (Combinatorial preparation); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); CMBI (Combinatorial study); PREP (Preparation); USES (Uses) (combinatorial preparation and pharmaceutical activity of substituted isophthalic acid derivs. as matrix metalloproteinase inhibitors) 1459-93-4P. Dimethyl isophthalate 4315-09-7P. 4-Nitroisophthalic acid 13756-42-8P, 4-Methylbenzoic acid tert-butyl ester 63746-12-3P, Dimethyl 4-aminoisophthalate 69048-70-0P, Dimethyl 4-nitroisophthalate 91360-95-1P 108052-76-2P, tert-Butyl-4-(bromomethyl)benzoate 175143-75-6P 177913-48-3P. Dimethyl 4-amino-1-hydroxycyclohexa-3,5-diene-1,3-dicarboxylate 209604-61-5P 221540-53-0P 342644-48-8P 448964-68-9P 448964-69-0P 448964-70-3P 449207-91-4P 449207-94-7P 449207-95-8P 449208-21-3P 449208-24-6P 449208-35-9P 449208-43-9P 449208-44-0P 449208-33-7P 449208-34-8P 449208-45-1P 449208-51-9P 449208-53-1P 449210-05-3P 449210-06-4P 449210-09-7P 449210-08-6P 449210-10-0P 449210-14-4P. 1-Benzyl-2,6-dioxo-1,2,3,6-tetrahydropyrimidine-4-carboxaldehyde 449210-15-5P 449210-16-6P 449210-17-7P 449210-18-8P 449210-19-9P 449755-90-2P 449210-21-3P 449210-22-4P 449211-37-4P 449211-38-5P 449755-91-3P 449755-92-4P 449755-95-7P 449755-96-8P 449798-65-6P 449798-69-0P 449798-67-8P. 6-Benzylthiazolo[3,2-c]pyrimidine-5,7-dione 449798-70-3P 449798-72-5P 449798-74-7P 449799-51-3P 449799-52-4P 449799-63-7P 449799-64-8P 451471-59-3P 451471-60-6P 451471-61-7P 451471-62-8P 451471-63-9P 451471-64-0P 451471-65-1P 451471-66-2P 451471-67-3P 451471-68-4P 451471-69-5P 451471-70-8P 451471-71-9P 451471-72-0P 451471-73-1P 451471-74-2P 451471-75-3P RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (intermediate: preparation and pharmaceutical activity of substituted isophthalic acid derivs.. multicyclic pyrimidinediones and analogs thereof as matrix metalloproteinase inhibitors)

9001-12-1, Matrix metalloproteinase-1 79955-99-0, Matrix

Page 23

```
metalloproteinase-3 141256-52-2. Matrix metalloproteinase-7 146480-35-5. Matrix metalloproteinase-2 146480-36-6. Matrix metalloproteinase-9 161384-17-4. Matrix metalloproteinase-14 175449-82-8. Collagenase 3
```

RL: BSU (Biological study, unclassified); BIOL (Biological study) (preparation and pharmaceutical activity of substituted isophthalic acid derivs., multicyclic pyrimidinediones and analogs thereof as matrix metalloproteinase inhibitors)

T 149277-46-3, GenBank A0000434

RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)

(preparation and pharmaceutical activity of substituted isophthalic acid derivs.. multicyclic pyrimidinediones and analogs thereof as matrix metalloproteinase inhibitors)

IT 100-46-9, Benzyl amine, reactions 104-86-9, 4-Chlorobenzyl amine
2393-23-9, 4-Methoxybenzylamine 2620-50-0, Piperonyl amine
RL: CRT (Combinatorial reactant); RCT (Reactant); CMBI (Combinatorial study); RACT (Reactant or reagent)

(preparation and pharmaceutical activity of substituted isophthalic acid derivs., multicyclic pyrimidinediones and analogs thereof as matrix metalloproteinase inhibitors)

IT 449792-10-3P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation and pharmaceutical activity of substituted isophthalic acid derivs.. multicyclic pyrimidinediones and analogs thereof as matrix metalloproteinase inhibitors)

96-33-3. Methyl acrylate 99-63-8, 1,3-Benzenedicarbonyl dichloride 100-11-8, 4-Nitrobenzylbromide 100-51-6, Benzyl alcohol, reactions 105-53-3, Diethylmalonate 108-90-7, Chlorobenzene, reactions 140-88-5, Ethyl acrylate 459-46-1, 4-Fluorobenzyl bromide 495-76-1, Piperonyl alcohol 501-53-1, Benzylchloroformate 538-32-9, Benzylurea 586-95-8, 4-Pyridinemethanol 609-08-5. Diethylmethyl malonate 623-51-8. Mercapto-acetic acid, ethyl ester 874-60-2, 4-Methylbenzoyl chloride 1189-71-5, N-Chlorosulfonyl isocyanate 2206-43-1, 4-Methoxy-1.3benzenedicarboxylic acid 2417-72-3, Methyl-4-(bromomethyl)benzoate 3113-72-2, 5-Methyl-2-nitrobenzoic acid 3173-56-6, Benzylisocyanate 3731-53-1, Pyridin-4-ylmethylamine 4392-24-9, Cinnamyl bromide 4637-24-5 5326-47-6. 2-Amino-5-iodobenzoic acid 6232-11-7. Methyl 4-(aminomethyl)benzoate, hydrochloride 6959-47-3, Picolyl chloride. hydrochloride 7149-10-2. 4-Hydroxy-3-methoxybenzylamine. hydrochloride 7252-83-7. Bromoacetaldehyde dimethylacetal 10147-11-2. 3-Phenyl-1-propyne 13235-60-4 13540-76-6, 3-(4-Methoxyphenyl)prop-1yne 17201-43-3, 4-(Bromomethyl)benzonitrile 18358-63-9. Methyl-4-methylaminobenzoate 18469-52-8. Methyl 4-(aminomethyl)benzoate 22600-30-2, Methyl-5-amino-2-furoate 25589-18-8, 3-Benzyl-6-methyl-1Hpyrimidine-2,4-dione 27757-85-3, 2-Thiophene methylamine 30280-44-5, 4-Chlorobenzyl isocyanate 40517-43-9, 4-Methylsulfonylbenzyl chloride 54751-01-8, 4-Bromomethylpyridine 56651-60-6, 4-Methoxybenzyl isocyanate 138895-24-6, 6-Amino-3-benzyl-1H-pyrimidine-2.4-dione 183741-86-8 305805-20-3 449208-54-2 449211-43-2 449798-87-2 305804-90-4 449799-49-9

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation and pharmaceutical activity of substituted isophthalic acid derivs., multicyclic pyrimidinediones and analogs thereof as matrix metalloproteinase inhibitors)

IT 449790-79-8P

RL: CPN (Combinatorial preparation): PAC (Pharmacological activity); SPN (Synthetic preparation): THU (Therapeutic use): BIOL (Biological study): CMBI (Combinatorial study): PREP (Preparation): USES (Uses)

(target compound: combinatorial preparation and pharmaceutical activity of substituted isophthalic acid derivs. as matrix metalloproteinase inhibitors)

Truong 10/075954 Page 24

```
449208-37-1P
                                                                   449208-39-3P
ΙT
     448964-75-8P
                    449208-01-9P
                                    449208-02-0P
                                    449208-57-5P
                                                    449211-17-0P
     449208-42-8P
                    449208-50-8P
    RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic.
    preparation): THU (Therapeutic use): BIOL (Biological study); PREP
     (Preparation): RACT (Reactant or reagent): USES (Uses)
        (target compound: preparation and pharmaceutical activity of substituted
        isophthalic acid derivs., multicyclic pyrimidinediones and analogs
        thereof as matrix metalloproteinase inhibitors)
                                                                  167993-08-0P
                                  151107-61-8P
                                                   152699-63-3P
IT
     16034-14-3P
                   143569-91-9P
                                    448964-76-9P
                                                    448964-82-7P
                                                                   448964-84-9P
                    383163-58-4P
     349396-68-5P
                                    448964-90-7P
                                                    448964-94-1P
                                                                   448964-98-5P
     448964-85-0P
                    448964-86-1P
                                                                   448965-36-4P
     448964-99-6P
                    448965-31-9P
                                    448965-33-1P
                                                    448965-35-3P
                                                                   448965-43-3P
                                    448965-41-1P
                                                    448965-42-2P
     448965-38-6P
                    448965-39-7P
                                    448965-47-7P
                                                    448965-48-8P
                                                                   448965-49-9P
                    448965-46-6P
     448965-44-4P
                                                    448965-58-0P
                                                                   448965-59-1P
     448965-50-2P
                    448965-51-3P
                                    448965-57-9P
                                                                   448965-69-3P
                    448965-64-8P
                                    448965-66-0P
                                                    448965-67-1P
     448965-60-4P
                                                    448965-73-9P
                                                                   448965-74-0P
                    448965-71-7P
                                    448965-72-8P
     448965-70-6P
                                                                   448965-79-5P
     448965-75-1P
                    448965-76-2P
                                    448965-77-3P
                                                    448965-78-4P
                                    448965-89-7P
                                                    448965-91-1P
                                                                   448965-93-3P
     448965-80-8P
                    448965-82-0P
                                                                   448966-00-5P
     448965-96-6P
                    448965-97-7P
                                    448965-98-8P
                                                    448965-99-9P
                                                    448966-04-9P
                                                                   448966-05-0P
                                    448966-03-8P
                    448966-02-7P
     448966-01-6P
                    448966-07-2P
                                    448966-09-4P
                                                    448966-10-7P
                                                                   448966-11-8P
     448966-06-1P
     448966-12-9P
                    448966-13-0P
                                    448966-14-1P
                                                    448966-15-2P
                                                                   448966-16-3P
                                                                   448966-23-2P
                                                    448966-22-1P
                    448966-19-6P
                                    448966-21-0P
     448966-17-4P
                                                    448966-27-6P
                                                                   448966-28-7P
                    448966-25-4P
                                    448966-26-5P
     448966-24-3P
                    448966-30-1P
                                                                   448966-33-4P
                                    448966-31-2P
                                                    448966-32-3P
     448966-29-8P
                                    448966-36-7P
                                                    448966-42-5P
                                                                   448966-45-8P
     448966-34-5P
                     448966-35-6P
     448966-50-5P
                     448966-52-7P
                                    448966-53-8P
                                                    448966-57-2P
                                                                   448966-65-2P
                                                    448966-75-4P
                                                                   448966-77-6P
     448966-68-5P
                     448966-71-0P
                                    448966-72-1P
                     448966-85-6P
                                    448966-86-7P
                                                    448966-87-8P
                                                                   448966-88-9P
     448966-78-7P
     448966-92-5P
                     448966-94-7P
                                    448966-95-8P
                                                    448966-96-9P
                                                                   448966-97-0P
                                                                   448967-08-6P
                                                    448967-07-5P
     448967-02-0P
                     448967-05-3P
                                    448967-06-4P
                                    448967-12-2P
                                                    448967-13-3P
                                                                   448967-14-4P
     448967-09-7P
                     448967-10-0P
                                    448967-20-2P
                                                    448967-21-3P
                                                                   448967-23-5P
     448967-16-6P
                     448967-19-9P
                     448967-25-7P
                                    448967-26-8P
                                                    448967-27-9P
                                                                   448967-28-0P
     448967-24-6P
                                    448967-31-5P
                                                    448967-34-8P
                                                                   448967-35-9P
     448967-29-1P
                     448967-30-4P
                                                    448967-44-0P
                                                                   448967-45-1P
                     448967-39-3P
                                    448967-41-7P
     448967-38-2P
                                                    448967-50-8P
                                                                   448967-52-0P
     448967-47-3P
                     448967-48-4P
                                    448967-49-5P
                     448967-54-2P
                                    448967-56-4P
                                                    448967-57-5P
                                                                   448967-59-7P
     448967-53-1P
                                                                   448967-66-6P
                                    448967-63-3P
                                                    448967-64-4P
                     448967-61-1P
     448967-60-0P
                     448967-71-3P
                                    448967-72-4P
                                                    448967-73-5P
                                                                   448967-74-6P
     448967-69-9P
                                    448967-81-5P
                                                    448967-82-6P
                                                                   448967-87-1P
     448967-76-8P
                     448967-80-4P
                                                                   448967-96-2P
     448967-88-2P
                     448967-92-8P
                                    448967-93-9P
                                                    448967-94-0P
                                    448967-99-5P
                                                    448968-00-1P
                                                                   448968-03-4P
                     448967-98-4P
     448967-97-3P
                     448968-12-5P
                                    448968-16-9P
                                                    448968-19-2P
                                                                   448968-23-8P
     448968-11-4P
                                    448968-28-3P
                                                    448968-30-7P
                                                                   448968-34-1P
     448968-24-9P
                     448968-27-2P
                                                                   448968-44-3P
     448968-35-2P
                     448968-40-9P
                                    448968-41-0P
                                                    448968-43-2P
                                                    448968-53-4P
                                                                   448968-54-5P
                                    448968-51-2P
     448968-45-4P
                     448968-49-8P
                                                                   449208-03-1P
                     448968-68-1P
                                    448968-69-2P
                                                    448970-24-9P
     448968-55-6P
     449208-04-2P
                     449208-06-4P
                                    449208-07-5P
                                                    449208-08-6P
                                                                   449208-09-7P
                                                    449208-13-3P
                                                                   449208-14-4P
     449208-10-0P
                     449208-11-1P
                                    449208-12-2P
                                    449208-20-2P
                                                    449208-22-4P
                                                                   449208-23-5P
                     449208-16-6P
     449208-15-5P
                                                                   449208-40-6P
     449208-26-8P
                     449208-32-6P
                                    449208-36-0P
                                                    449208-38-2P
                                    449208-47-3P
                                                    449208-48-4P
                                                                   449208-49-5P
     449208-41-7P
                     449208-46-2P
                                                    449208-59-7P
                                                                   449208-60-0P
     449208-52-0P
                    449208-55-3P
                                    449208-58-6P
     RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
     (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
     (Uses)
        (target compound: preparation and pharmaceutical activity of substituted
        isophthalic acid derivs., multicyclic pyrimidinediones and analogs
        thereof as matrix metalloproteinase inhibitors)
                                                    449208-64-4P
                                                                   449208-65-5P
     449208-61-1P
                     449208-62-2P
                                    449208-63-3P
                     449208-69-9P
                                    449208-70-2P
                                                    449208-71-3P
                                                                   449208-72-4P
     449208-66-6P
                                                    449208-76-8P
                                                                   449208-77-9P
     449208-73-5P
                    449208-74-6P
                                    449208-75-7P
```

Truong 10/075954 Page 25

449208-82-6P

449208-81-5P

```
449208-87-1P
                                                              449208-88-2P
                               449208-85-9P
449208-83-7P
               449208-84-8P
               449208-90-6P
                               449208-91-7P
                                               449208-92-8P
                                                              449208-93-9P
449208-89-3P
449208-94-0P
               449208-95-1P
                               449208-96-2P
                                               449208-97-3P
                                                              449208-98-4P
                                                              449209-07-8P
                                               449209-06-7P
449208-99-5P
               449209-00-1P
                               449209-01-2P
                               449209-14-7P
                                               449209-16-9P
                                                              449209-17-0P
               449209-13-6P
449209-09-0P
                                                              449209-22-7P
               449209-19-2P
                               449209-20-5P
                                               449209-21-6P
449209-18-1P
               449209-24-9P
                               449209-25-0P
                                               449209-26-1P
                                                              449209-27-2P
449209-23-8P
                               449209-30-7P
                                               449209-31-8P
                                                              449209-32-9P
449209-28-3P
               449209-29-4P
                               449209-36-3P
                                               449209-37-4P
                                                              449209-39-6P
               449209-34-1P
449209-33-0P
449209-40-9P
                                                              449209-45-4P
               449209-41-0P
                               449209-43-2P
                                               449209-44-3P
449209-46-5P
               449209-47-6P
                               449209-48-7P
                                               449209-49-8P
                                                              449209-52-3P
                               449209-59-0P
                                               449209-60-3P
                                                              449209-61-4P
449209-53-4P
               449209-54-5P
                                               449209-66-9P
                                                              449209-67-0P
                               449209-65-8P
449209-63-6P
               449209-64-7P
                                                              449209-72-7P
449209-68-1P
               449209-69-2P
                               449209-70-5P
                                               449209-71-6P
               449209-77-2P
                               449209-79-4P
                                               449209-81-8P
                                                              449209-82-9P
449209-75-0P
                                                              449209-90-9P
449209-83-0P
               449209-84-1P
                               449209-86-3P
                                               449209-89-6P
                               449209-97-6P
                                               449209-98-7P
                                                              449209-99-8P
449209-91-0P
               449209-94-3P
                                                              449210-11-1P
               449210-01-9P
                               449210-03-1P
                                               449210-07-5P
449210-00-8P
449210-12-2P 449210-13-3P 449210-20-2P
                                             449210-29-1P
449210-24-6P 449210-27-9P
                             449210-28-0P
                               449210-32-6P
                                               449210-33-7P
                                                              449210-34-8P
449210-30-4P
               449210-31-5P
449210-36-0P
               449210-37-1P
                               449210-38-2P
                                               449210-39-3P
                                                              449210-40-6P
               449210-42-8P
                               449210-45-1P
                                            449210-47-3P
449210-41-7P
                                                              449210-54-2P
                               449210-52-0P
                                               449210-53-1P
449210-49-5P
               449210-51-9P
                                               449210-61-1P
                               449210-57-5P
                                                              449210-62-2P
449210-55-3P
               449210-56-4P
                                               449210-72-4P
                                                              449210-74-6P
               449210-67-7P
                               449210-68-8P
449210-66-6P
               449210-76-8P
                               449210-78-0P
                                               449210-79-1P
                                                              449210-81-5P
449210-75-7P
                                                              449210-88-2P
449210-82-6P
               449210-84-8P
                               449210-85-9P
                                               449210-87-1P
                                               449210-96-2P
                                                              449210-97-3P
               449210-90-6P
                               449210-95-1P
449210-89-3P
               449211-03-4P
                               449211-04-5P
                                               449211-05-6P
                                                              449211-06-7P
449211-02-3P
               449211-08-9P
                               449211-09-0P
                                               449211-10-3P
                                                              449211-11-4P
449211-07-8P
                               449211-15-8P
                                               449211-16-9P
                                                              449211-18-1P
449211-13-6P
               449211-14-7P
               449211-20-5P
                               449211-21-6P
                                               449211-22-7P
                                                              449211-24-9P
449211-19-2P
                                               449211-29-4P
                                                              449211-30-7P
449211-25-0P
               449211-27-2P
                               449211-28-3P
               449211-32-9P
                               449211-33-0P
                                               449211-34-1P
                                                              449211-35-2P
449211-31-8P
                                                              449754-53-4P
                               449754-50-1P
                                               449754-51-2P
449211-36-3P
               449754-49-8P
449754-59-0P
               449754-61-4P
                               449754-62-5P
                                               449754-64-7P
                                                              449754-65-8P
                                               449754-70-5P
                                                              449754-72-7P
449754-66-9P
               449754-67-0P
                               449754-69-2P
                                                              449754-77-2P
449754-73-8P
               449754-74-9P
                               449754-75-0P
                                               449754-76-1P
               449754-79-4P
                               449754-80-7P
                                               449754-82-9P
                                                              449754-83-0P
449754-78-3P
                                                              449754-88-5P
449754-84-1P
               449754-85-2P
                               449754-86-3P
                                               449754-87-4P
449754-89-6P
               449754-97-6P
                               449754-99-8P
                                               449790-17-4P
                                                              449790-22-1P
                                                              449790-39-0P
449790-25-4P
               449790-28-7P
                               449790-33-4P
                                               449790-36-7P
               449790-45-8P
                               449790-52-7P
                                               449790-57-2P
449790-42-5P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation): THU
(Therapeutic use): BIOL (Biological study); PREP (Preparation); USES
(Uses)
   (target compound: preparation and pharmaceutical activity of substituted
   isophthalic acid derivs., multicyclic pyrimidinediones and analogs
   thereof as matrix metalloproteinase inhibitors)
                                                              449790-95-8P
                               449790-70-9P
                                               449790-87-8P
449790-60-7P
               449790-66-3P
                               449791-04-2P
449790-98-1P
               449791-01-9P
                                               449791-09-7P
                                                              449791-12-2P
                               449791-20-2P
                                               449791-28-0P
                                                              449791-31-5P
449791-15-5P
               449791-18-8P
                                                               449791-53-1P
               449791-44-0P
                               449791-47-3P
                                               449791-50-8P
449791-41-7P
                                               449791-65-5P
                                                              449791-68-8P
449791-56-4P
               449791-59-7P
                               449791-62-2P
               449791-74-6P
                               449791-77-9P
                                               449791-81-5P
                                                               449791-84-8P
449791-71-3P
                               449791-96-2P
                                               449791-99-5P
                                                               449792-02-3P
449791-90-6P
               449791-93-9P
                                                               449798-68-9P
449792-04-5P
               449792-07-8P
                               449792-13-6P
                                               449798-64-5P
                                                               449798-82-7P
                               449798-80-5P
                                               449798-81-6P
               449798-75-8P
449798-71-4P
                                                               449798-94-1P
449798-86-1P
               449798-88-3P
                               449798-90-7P
                                               449798-91-8P
               449798-97-4P
                               449799-02-4P
                                               449799-05-7P
                                                               449799-06-8P
449798-95-2P
                               449799-19-3P
                                               449799-27-3P
                                                               449799-34-2P
449799-14-8P
               449799-16-0P
449799-36-4P
               449799-37-5P
                               449799-38-6P
                                               449799-40-0P
                                                               449799-42-2P
```

449208-78-0P

449208-79-1P

449208-80-4P

Page 26 Truong 10/075954

```
449799-50-2P
                                                            449799-53-5P
449799-43-3P
               449799-44-4P
                              449799-45-5P
                                             449799-60-4P
                                                            449799-62-6P
449799-55-7P
               449799-58-0P
                              449799-59-1P
449799-65-9P
               449799-66-0P
                              449799-67-1P
                                             449799-70-6P
                                                            449799-71-7P
                                                            449799-77-3P
449799-72-8P
               449799-73-9P
                              449799-74-0P
                                             449799-76-2P
                                                            449799-84-2P
                              449799-80-8P
                                             449799-81-9P
449799-78-4P
               449799-79-5P
               449799-86-4P
449799-85-3P
                              449799-87-5P
                                             449799-89-7P
                                                            449799-90-0P
                              449799-97-7P
                                             449799-98-8P
                                                            449800-01-5P
449799-93-3P
               449799-96-6P
               449800-04-8P
                              449800-05-9P
                                             449800-07-1P
                                                            449800-08-2P
449800-03-7P
                                                            449800-19-5P
                              449800-13-9P
                                             449800-15-1P
449800-09-3P
               449800-12-8P
               451471-32-2P
                              451471-33-3P
                                             451471-34-4P
                                                            451471-35-5P
451471-31-1P
                                             451471-39-9P.
451471-36-6P
               451471-37-7P
                              451471-38-8P
Thieno[2,3-d]pyrimidine-6-carboxylic acid benzyl ester 451471-40-2P
                                                            451471-45-7P
               451471-42-4P
                              451471-43-5P
                                             451471-44-6P
451471-41-3P
               451471-48-0P
                              451471-49-1P
                                             451471-50-4P
                                                            451471-51-5P
451471-47-9P
                              451471-54-8P
                                             451471-55-9P
                                                            451471-56-0P
451471-52-6P
              451471-53-7P
451471-57-1P
              451471-58-2P
                              451473-18-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
```

(target compound: preparation and pharmaceutical activity of substituted isophthalic acid derivs., multicyclic pyrimidinediones and analogs thereof as matrix metalloproteinase inhibitors)

452379-12-3

RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)

(unclaimed protein sequence; preparation and pharmaceutical activity of substituted isophthalic acid derivs.. multicyclic pyrimidinediones and analogs thereof as matrix metalloproteinase inhibitors)

449210-13-3P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES

(target compound; preparation and pharmaceutical activity of substituted isophthalic acid derivs., multicyclic pyrimidinediones and analogs thereof as matrix metalloproteinase inhibitors)

449210-13-3 HCAPLUS

 ${\tt Pyrido[3.4-d]pyrimidine-6-carboxamide. N-(1.3-benzodioxol-5-ylmethyl)-}$ 1.2.3.4-tetrahydro-1-methyl-2.4-dioxo-3-(phenylmethyl)- (9CI) (CA INDEX

=> b home

FILE 'HOME' ENTERED AT 11:48:16 ON 07 FEB 2005

 $C_{26}H_{24}N_4O_6$

$$\begin{array}{c|c} & C_{25}H_{22}N_4O_6 & \text{MeO} \\ & & \\ & & \\ O & & \\ & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ &$$

 $C_{25}H_{22}N_4O_6$

 $C_{25}H_{21}N_5O_4$

=> b reg

FILE 'REGISTRY' ENTERED AT 13:41:49 ON 07 FEB 2005 USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT. PLEASE SEE "HELP USAGETERMS" FOR DETAILS. COPYRIGHT (C) 2005 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 6 FEB 2005 HIGHEST RN 826990-02-7 DICTIONARY FILE UPDATES: 6 FEB 2005 HIGHEST RN 826990-02-7

TSCA INFORMATION NOW CURRENT THROUGH MAY 21, 2004

Please note that search-term pricing does apply when conducting ${\tt SmartSELECT}$ searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at: http://www.cas.org/ONLINE/DBSS/registryss.html

=> d ide 125 tot

L25 ANSWER 1 OF 7 REGISTRY COPYRIGHT 2005 ACS on STN

RN 449210-47-3 REGISTRY

CN Benzoic acid. 4-[[1.4-dihydro-6-[[[(4-methoxyphenyl)methyl]amino]carbonyl]1-methyl-2.4-dioxopyrido[3.4-d]pyrimidin-3(2H)-yl]methyl]- (9CI) (CA
INDEX NAME)

OTHER NAMES:

CN 4-[[6-(4-Methoxybenzylcarbamoyl)-1-methyl-2.4-dioxo-1.4-dihydro-2H-pyrido[3.4-d]pyrimidin-3-yl]methyl]benzoic acid

FS 3D CONCORD

MF C25 H22 N4 O6

SR CA

LC STN Files: CA, CAPLUS, CASREACT, TOXCENTER, USPATFULL

DT.CA CAplus document type: Patent

RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

4 REFERENCES IN FILE CA (1907 TO DATE)
4 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L25 ANSWER 2 OF 7 REGISTRY COPYRIGHT 2005 ACS on STN

RN 449210-27-9 REGISTRY

CN Pyrido[3.4-d]pyrimidine-6-carboxamide. 3-[(4-cyanophenyl)methyl]-1.2.3.4-tetrahydro-N-[(4-methoxyphenyl)methyl]-1-methyl-2.4-dioxo- (9CI) (CA INDEX NAME)

FS 3D CONCORD

MF C25 H21 N5 O4

SR CA

LC STN Files: CA, CAPLUS, CASREACT, TOXCENTER, USPATFULL

DT.CA CAplus document type: Patent

RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

4 REFERENCES IN FILE CA (1907 TO DATE)

4 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L25 ANSWER 3 OF 7 REGISTRY COPYRIGHT 2005 ACS on STN

RN 449210-24-6 REGISTRY

CN Benzoic acid. 4-[[1.4-dihydro-6-[[[(3-methoxyphenyl)methyl]amino]carbonyl]1-methyl-2,4-dioxopyrido[3,4-d]pyrimidin-3(2H)-yl]methyl]- (9CI) (CA
INDEX NAME)

OTHER NAMES:

CN 4-[[6-(3-Methoxybenzylcarbamoyl)-1-methyl-2.4-dioxo-1,4-dihydro-2H-pyrido[3,4-d]pyrimidin-3-yl]methyl]benzoic acid

FS 3D CONCORD

MF C25 H22 N4 06

SR CA

LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

DT.CA CAplus document type: Patent

RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

4 REFERENCES IN FILE CA (1907 TO DATE)

4 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L25 ANSWER 4 OF 7 REGISTRY COPYRIGHT 2005 ACS on STN

RN 449210-20-2 REGISTRY

CN Benzoic acid. 4-[[1,4-dihydro-6-[[[(4-methoxyphenyl)methyl]amino]carbonyl]1-methyl-2,4-dioxopyrido[3,4-d]pyrimidin-3(2H)-yl]methyl]-, methyl ester
(9CI) (CA INDEX NAME)

OTHER NAMES:

CN Methyl 4-[[6-(4-Methoxybenzylcarbamoyl)-1-methyl-2,4-dioxo-1,4-dihydro-2H-pyrido[3,4-d]pyrimidin-3-yl]methyl]benzoate

FS 3D CONCORD

MF C26 H24 N4 06

SR CA

LC STN Files: CA, CAPLUS, CASREACT, TOXCENTER, USPATFULL

DT.CA CAplus document type: Patent

RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

4 REFERENCES IN FILE CA (1907 TO DATE)

4 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L25 ANSWER 5 OF 7 REGISTRY COPYRIGHT 2005 ACS on STN

RN 449210-11-1 REGISTRY

CN Pyrido[2,3-d]pyrimidine-6-carboxamide, 3-[(4-cyanophenyl)methyl]-1.2,3,4-tetrahydro-N-[(4-methoxyphenyl)methyl]-1-methyl-2,4-dioxo- (9CI) (CA INDEX NAME)

FS 3D CONCORD

MF C25 H21 N5 O4

SR CA

LC STN Files: CA, CAPLUS, CASREACT, TOXCENTER, USPATFULL

DT.CA CAplus document type: Patent

RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L25 ANSWER 6 OF 7 REGISTRY COPYRIGHT 2005 ACS on STN

RN 449210-10-0 REGISTRY

CN Benzoic acid. 4-[[1.4-dihydro-6-[[[(4-methoxyphenyl)methyl]amino]carbonyl]-1-methyl-2.4-dioxopyrido[2,3-d]pyrimidin-3(2H)-yl]methyl]-. methyl ester (9CI) (CA INDEX NAME)

OTHER NAMES:

CN Methyl 4-[[6-(4-Methoxybenzylcarbamoyl)-1-methyl-2.4-dioxo-1.4-dihydro-2H-pyrido[2,3-d]pyrimidin-3-yl]methyl]benzoate

FS 3D CONCORD

MF C26 H24 N4 O6

SR CA

LC STN Files: CA, CAPLUS, CASREACT, TOXCENTER, USPATFULL

DT.CA CAplus document type: Patent

RL.P Roles from patents: PREP (Preparation); RACT (Reactant or reagent)

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L25 ANSWER 7 OF 7 REGISTRY COPYRIGHT 2005 ACS on STN

RN 449210-07-5 REGISTRY

CN Benzoic acid. 4-[[1.4-dihydro-6-[[[(4-methoxyphenyl)methyl]amino]carbonyl]1-methyl-2.4-dioxopyrido[2.3-d]pyrimidin-3(2H)-yl]methyl]- (9CI) (CA
INDEX NAME)

OTHER NAMES:

CN 4-[[6-(4-Methoxybenzylcarbamoyl)-1-methyl-2.4-dioxo-1,4-dihydro-2H-pyrido[2,3-d]pyrimidin-3-yl]methyl]benzoic acid

FS 3D CONCORD

MF C25 H22 N4 O6

SR CA

LC STN Files: CA, CAPLUS, CASREACT, TOXCENTER, USPATFULL

DT.CA CAplus document type: Patent

RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

4 REFERENCES IN FILE CA (1907 TO DATE)
4 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> d his

(FILE 'HOME' ENTERED AT 11:20:28 ON 07 FEB 2005)

FILE 'HCAPLUS' ENTERED AT 11:20:35 ON 07 FEB 2005

L1 1 US20020193377/PN

E US2001-268661/AP.PRN

L2 1 US2001-268661P/AP.PRN

L3 1 L1-2

FILE 'REGISTRY' ENTERED AT 11:21:44 ON 07 FEB 2005

FILE 'HCAPLUS' ENTERED AT 11:21:46 ON 07 FEB 2005 L4 TRA L3 1- RN : 441 TERMS

FILE 'REGISTRY' ENTERED AT 11:21:48 ON 07 FEB 2005 L5 441 SEA L4

```
FILE 'WPIX' ENTERED AT 11:21:54 ON 07 FEB 2005
L6
              1 US20020193377/PN
              1 US2001-268661P/AP.PRN
L7
                E US2001-268661/AP, PRN
L8
              1 L6-7
     FILE 'HCAPLUS' ENTERED AT 11:22:40 ON 07 FEB 2005
     FILE 'WPIX' ENTERED AT 11:22:53 ON 07 FEB 2005
     FILE 'HOME' ENTERED AT 11:23:05 ON 07 FEB 2005
     FILE 'STNGUIDE' ENTERED AT 11:23:25 ON 07 FEB 2005
     FILE 'REGISTRY' ENTERED AT 11:35:05 ON 07 FEB 2005
L9
                STR
              0 L9
L10
L11
                STR L9
L12
              0 L11
L13
                STR L11
L14
              0 L13
L15
              7 L13 FULL
                SAV TEM L15 TRU954F0/A
     FILE 'HCAPLUS' ENTERED AT 11:45:42 ON 07 FEB 2005
L16
              4 L15
     FILE 'HCAOLD' ENTERED AT 11:45:49 ON 07 FEB 2005
L17
              0 L15
     FILE 'REGISTRY' ENTERED AT 12:38:36 ON 07 FEB 2005
L18
            168 L5 AND METHOXY
L19
            147 L18 AND 2(1A) 4 (1A) DIOXO
     FILE 'STNGUIDE' ENTERED AT 12:45:00 ON 07 FEB 2005
     FILE 'REGISTRY' ENTERED AT 13:05:15 ON 07 FEB 2005
L20
             53 BENZYLCARBAMOYL AND L5
L21
              4 L5 AND 3(1A) 4(1A) CYANO
     FILE 'STNGUIDE' ENTERED AT 13:15:47 ON 07 FEB 2005
     FILE 'REGISTRY' ENTERED AT 13:38:03 ON 07 FEB 2005
L22
            626 C26H24N4O6 OR C25H22N4O6 OR C25H22N4O6 OR C25H21N5O4
L23
            315 L22 AND NR=4
L24
              9 NCNC3-NC5/ES AND L23
                SEL RN 2-8
L25
              7 E1-7 AND L24
     FILE 'HCAPLUS' ENTERED AT 13:43:10 ON 07 FEB 2005
L26
              4 L25
=> b hcap
FILE 'HCAPLUS' ENTERED AT 13:43:39 ON 07 FEB 2005
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2005 AMERICAN CHEMICAL SOCIETY (ACS)
```

Copyright of the articles to which records in this database refer is held by the publishers listed in the PUBLISHER (PB) field (available for records published or updated in Chemical Abstracts after December 26. 1996), unless otherwise indicated in the original publications.

The CA Lexicon is the copyrighted intellectual property of the the American Chemical Society and is provided to assist you in searching databases on STN. Any dissemination, distribution, copying, or storing of this information, without the prior written consent of CAS, is strictly prohibited.

FILE COVERS 1907 - 7 Feb 2005 VOL 142 ISS 7 FILE LAST UPDATED: 6 Feb 2005 (20050206/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

```
=> => d all hitstr 126 tot
```

Ampuls

```
L26 ANSWER 1 OF 4 HCAPLUS COPYRIGHT 2005 ACS on STN
    2004:60320 HCAPLUS
AN
    140:105336
    Entered STN: 26 Jan 2004
    Combination of an allosteric carboxylic inhibitor of matrix
     metalloproteinase-13 with a selective inhibitor of cyclooxygenase-2 that
     is not celecoxib or valdecoxib, and therapeutic use
ΙN
     Roark, William Howard
    Warner-Lambert Company LLC, USA
PA
    PCT Int. Appl., 239 pp.
     CODEN: PIXXD2
DT
    Patent
ΙA
     English
    ICM A61K031-519
     ICS A61K031-00; A61P019-02; A61P009-00
     1-12 (Pharmacology)
FAN.CNT 1
     PATENT NO.
                         KIND DATE
                                            APPLICATION NO.
                                                                    DATE
                                20040122
                                                                    20030707
PΙ
    WO 2004006931
                          A2
                                            WO 2003-IB3098
     WO 2004006931
                         A3
                                20040513
        W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,
             PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT,
             TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
             KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
             BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
     US 2004019054
                          A1
                                20040129
                                            US 2003-619769
                                                                    20030715
PRAI US 2002-396785P
                          Ρ
                                20020717
CLASS.
 PATENT NO.
                 CLASS PATENT FAMILY CLASSIFICATION CODES
 -----
 WO 2004006931
               ICM
                        A61K031-519
                        A61K031-00: A61P019-02: A61P009-00
                 ICS
OS
    MARPAT 140:105336
AB
    The invention provides a combination comprising an allosteric carboxylic
     inhibitor of MMP-13, or a pharmaceutically acceptable salt thereof, with a
     selective inhibitor of COX-2, or a pharmaceutically acceptable salt
     thereof, that is not celecoxib or valdecoxib, and their use for the
     treatment of diseases that are responsive to inhibition of MMP-13 and
     cyclooxygenase-2.
   cyclooxygenase 2 inhibitor MMP13 allosteric carboxylic inhibitor
     combination therapeutic; matrix metalloproteinase 13 inhibitor
     cyclooxygenase 2 inhibitor combination therapeutic
```

Analgesics Anti-inflammatory agents Antiarthritics Antirheumatic agents Drug delivery systems Inflammation Osteoarthritis Pain Rheumatoid arthritis (allosteric carboxylic inhibitor of matrix metalloproteinase-13 combination with selective inhibitor of cyclooxygenase-2 that is not celecoxib or valdecoxib, and therapeutic use) Drug delivery systems (capsules: allosteric carboxylic inhibitor of matrix metalloproteinase-13 combination with selective inhibitor of cyclooxygenase-2 that is not celecoxib or valdecoxib, and therapeutic use) Cartilage, disease (damage; allosteric carboxylic inhibitor of matrix metalloproteinase-13 combination with selective inhibitor of cyclooxygenase-2 that is not celecoxib or valdecoxib, and therapeutic use) IT Drug delivery systems (injections; allosteric carboxylic inhibitor of matrix metalloproteinase-13 combination with selective inhibitor of cyclooxygenase-2 that is not celecoxib or valdecoxib, and therapeutic use) IT Drug delivery systems (ointments; allosteric carboxylic inhibitor of matrix metalloproteinase-13 combination with selective inhibitor of cyclooxygenase-2 that is not celecoxib or valdecoxib, and therapeutic use) IT Drug delivery systems (solns.; allosteric carboxylic inhibitor of matrix metalloproteinase-13 combination with selective inhibitor of cyclooxygenase-2 that is not celecoxib or valdecoxib, and therapeutic use) Drug delivery systems (suppositories: allosteric carboxylic inhibitor of matrix metalloproteinase-13 combination with selective inhibitor of cyclooxygenase-2 that is not celecoxib or valdecoxib, and therapeutic use) Drug delivery systems (tablets, coated; allosteric carboxylic inhibitor of matrix metalloproteinase-13 combination with selective inhibitor of cyclooxygenase-2 that is not celecoxib or valdecoxib, and therapeutic use) IT Drug delivery systems (tablets; allosteric carboxylic inhibitor of matrix metalloproteinase-13 combination with selective inhibitor of cyclooxygenase-2 that is not celecoxib or valdecoxib, and therapeutic use) 175449-82-8, Matrix metalloproteinase 13 329900-75-6, Cyclooxygenase 2 RL: BSU (Biological study, unclassified); BIOL (Biological study) (allosteric carboxylic inhibitor of matrix metalloproteinase-13 combination with selective inhibitor of cyclooxygenase-2 that is not celecoxib or valdecoxib, and therapeutic use) 449210-07-5 449210-13-3 449210-20-2 449210-24-6 449210-27-9 449210-47-3 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (allosteric carboxylic inhibitor of matrix metalloproteinase-13 combination with selective inhibitor of cyclooxygenase-2 that is not celecoxib or valdecoxib, and therapeutic use)

IT 449210-07-5 449210-20-2 449210-24-6 449210-27-9 449210-47-3

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(allosteric carboxylic inhibitor of matrix metalloproteinase-13 combination with selective inhibitor of cyclooxygenase-2 that is not celecoxib or valdecoxib, and therapeutic use)

RN 449210-07-5 HCAPLUS

CN Benzoic acid. 4-[[1,4-dihydro-6-[[[(4-methoxyphenyl)methyl]amino]carbonyl]1-methyl-2.4-dioxopyrido[2,3-d]pyrimidin-3(2H)-yl]methyl]- (9CI) (CA
INDEX NAME)

RN 449210-20-2 HCAPLUS

CN Benzoic acid, 4-[[1.4-dihydro-6-[[[(4-methoxyphenyl)methyl]amino]carbonyl]1-methyl-2.4-dioxopyrido[3,4-d]pyrimidin-3(2H)-yl]methyl]-, methyl ester
(9CI) (CA INDEX NAME)

RN 449210-24-6 HCAPLUS

CN Benzoic acid. 4-[[1.4-dihydro-6-[[[(3-methoxyphenyl)methyl]amino]carbonyl]1-methyl-2.4-dioxopyrido[3.4-d]pyrimidin-3(2H)-yl]methyl]- (9CI) (CA
INDEX NAME)

RN 449210-27-9 HCAPLUS

CN Pyrido[3.4-d]pyrimidine-6-carboxamide, 3-[(4-cyanophenyl)methyl]-1.2.3.4-tetrahydro-N-[(4-methoxyphenyl)methyl]-1-methyl-2,4-dioxo- (9CI) (CA INDEX NAME)

RN 449210-47-3 HCAPLUS

CN Benzoic acid. 4-[[1.4-dihydro-6-[[[(4-methoxyphenyl)methyl]amino]carbonyl]-1-methyl-2.4-dioxopyrido[3.4-d]pyrimidin-3(2H)-yl]methyl]- (9CI) (CA INDEX NAME)

```
L26 ANSWER 2 OF 4 HCAPLUS COPYRIGHT 2005 ACS on STN
     2004:60302 HCAPLUS
AN
     140:105333
DN
     Entered STN: 26 Jan 2004
ED
     Combination of an allosteric carboxylic inhibitor of matrix
ΤI
     metalloproteinase-13 with celecoxib or valdecoxib, pharmaceutical
     compositions, and therapeutic use
IN
     Roark, William Howard
     Warner-Lambert Company LLC, USA
РΔ
S0
     PCT Int. Appl., 238 pp.
     CODEN: PIXXD2
DT
     Patent
ΙA
     English
     ICM A61K031-415
IC
     ICS A61K031-44; A61K031-42; A61K031-519
CC
     1-12 (Pharmacology)
     Section cross-reference(s): 63
FAN.CNT 1
                                                                     DATE
                                             APPLICATION NO.
     PATENT NO.
                          KIND
                                 DATE
                          ----
     WO 2004006912
                           A2
                                 20040122
                                             WO 2003-IB3044
                                                                     20030707
PΤ
     WO 2004006912
                           Α3
                                 20040603
         W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH.
             GM. HR. HU, ID. IL, IN, IS. JP. KE. KG. KP. KR. KZ. LC. LK. LR. LS. LT. LU, LV. MA. MD, MG, MK. MN, MW, MX. MZ. NI, NO, NZ. OM.
             PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT,
             TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: GH. GM. KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
              KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
             FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR.
              BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
     US 2004019053
                                 20040129
                                             US 2003-619662
                                                                     20030715
                           Α1
PRAI US 2002-396903P
                                 20020717
                           P
CLASS
                  CLASS PATENT FAMILY CLASSIFICATION CODES
 PATENT NO.
 WO 2004006912
                  ICM
                         A61K031-415
                  ICS
                         A61K031-44: A61K031-42: A61K031-519
     MARPAT 140:105333
     The invention provides a combination comprising an allosteric carboxylic
AB
     inhibitor of MMP-13, or a pharmaceutically acceptable salt thereof, with
     celecoxib, or a pharmaceutically acceptable salt thereof, or valdecoxib.
     or a pharmaceutically acceptable salt thereof. The invention also
     provides a method of treating a disease that is responsive to inhibition
     of MMP-13 and cyclooxygenase 2, comprising administering to a patient
     suffering from such a disease the invention combination comprising an
     allosteric carboxylic inhibitor of MMP-13, or a pharmaceutically
     acceptable salt thereof, with celecoxib, or a pharmaceutically acceptable
```

salt thereof, or valdecoxib, or a pharmaceutically acceptable salt

thereof. The invention also provides a pharmaceutical composition, comprising the invention combination comprising an allosteric carboxylic inhibitor of

MMP-13. or a pharmaceutically acceptable salt thereof, with celecoxib, or a pharmaceutically acceptable salt thereof, or valdecoxib, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier, diluent, or excipient. The invention combination may also be further combined with other pharmaceutical agents depending on the disease being treated.

ST allosteric carboxylic inhibitor matrix metalloproteinase 13 celecoxib valdecoxib therapeutic; MMP13 allosteric carboxylic inhibitor celecoxib valdecoxib combination therapeutic

IT Ampuls

Analgesics

Anti-inflammatory agents

Antiarthritics

Antirheumatic agents

Drug delivery systems

Human

Inflammation

Osteoarthritis

Pain

Rheumatoid arthritis

(allosteric carboxylic inhibitor of matrix metalloproteinase-13 combination with celecoxib or valdecoxib. pharmaceutical compns., and therapeutic use)

IT Drug delivery systems

(capsules: allosteric carboxylic inhibitor of matrix metalloproteinase-13 combination with celecoxib or valdecoxib, pharmaceutical compns., and therapeutic use)

IT Cartilage, disease

(damage: allosteric carboxylic inhibitor of matrix metalloproteinase-13 combination with celecoxib or valdecoxib, pharmaceutical compns., and therapeutic use)

IT Drug delivery systems

(injections; allosteric carboxylic inhibitor of matrix metalloproteinase-13 combination with celecoxib or valdecoxib, pharmaceutical compns., and therapeutic use)

IT Drug delivery systems

(ointments: allosteric carboxylic inhibitor of matrix metalloproteinase-13 combination with celecoxib or valdecoxib. pharmaceutical compns.. and therapeutic use)

IT Arthritis

(psoriatic arthritis; allosteric carboxylic inhibitor of matrix metalloproteinase-13 combination with celecoxib or valdecoxib. pharmaceutical compns.. and therapeutic use)

IT Drug delivery systems

(solns.: allosteric carboxylic inhibitor of matrix metalloproteinase-13 combination with celecoxib or valdecoxib, pharmaceutical compns., and therapeutic use)

IT Drug delivery systems

(suppositories; allosteric carboxylic inhibitor of matrix metalloproteinase-13 combination with celecoxib or valdecoxib, pharmaceutical compns., and therapeutic use)

IT Drug delivery systems

(tablets. coated: allosteric carboxylic inhibitor of matrix metalloproteinase-13 combination with celecoxib or valdecoxib, pharmaceutical compns., and therapeutic use)

IT Drug delivery systems

(tablets; allosteric carboxylic inhibitor of matrix metalloproteinase-13 combination with celecoxib or valdecoxib, pharmaceutical compns., and therapeutic use)

IT 175449-82-8, Matrix metalloproteinase 13

RL: BSU (Biological study, unclassified); BIOL (Biological study) (allosteric carboxylic inhibitor of matrix metalloproteinase-13 combination with celecoxib or valdecoxib, pharmaceutical compns., and therapeutic use)

IT 169590-42-5, Celecoxib 181695-72-7, Valdecoxib 449210-07-5

449210-13-3 449210-20-2 449210-24-6

449210-27-9 449210-47-3

RL: PAC (Pharmacological activity): THU (Therapeutic use); BIOL

(Biological study): USES (Uses)

(allosteric carboxylic inhibitor of matrix metalloproteinase-13 combination with celecoxib or valdecoxib, pharmaceutical compns., and therapeutic use)

IT 449210-07-5 449210-20-2 449210-24-6

449210-27-9 449210-47-3

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL

(Biological study); USES (Uses)

(allosteric carboxylic inhibitor of matrix metalloproteinase-13 combination with celecoxib or valdecoxib, pharmaceutical compns., and therapeutic use)

RN 449210-07-5 HCAPLUS

CN Benzoic acid. 4-[[1.4-dihydro-6-[[[(4-methoxyphenyl)methyl]amino]carbonyl]1-methyl-2.4-dioxopyrido[2,3-d]pyrimidin-3(2H)-yl]methyl]- (9CI) (CA
INDEX NAME)

RN 449210-20-2 HCAPLUS

CN Benzoic acid, 4-[[1.4-dihydro-6-[[[(4-methoxyphenyl)methyl]amino]carbonyl]-1-methyl-2,4-dioxopyrido[3,4-d]pyrimidin-3(2H)-yl]methyl]-, methyl ester (9CI) (CA INDEX NAME)

RN 449210-24-6 HCAPLUS

CN Benzoic acid, 4-[[1,4-dihydro-6-[[[(3-methoxyphenyl)methyl]amino]carbonyl]1-methyl-2,4-dioxopyrido[3,4-d]pyrimidin-3(2H)-yl]methyl]- (9CI) (CAINDEX NAME)

RN 449210-27-9 HCAPLUS

CN Pyrido[3.4-d]pyrimidine-6-carboxamide, 3-[(4-cyanophenyl)methyl]-1,2,3,4-tetrahydro-N-[(4-methoxyphenyl)methyl]-1-methyl-2,4-dioxo- (9CI) (CA INDEX NAME)

RN 449210-47-3 HCAPLUS

CN Benzoic acid. 4-[[1.4-dihydro-6-[[[(4-methoxyphenyl)methyl]amino]carbonyl]1-methyl-2.4-dioxopyrido[3.4-d]pyrimidin-3(2H)-yl]methyl]- (9CI) (CA
INDEX NAME)

L26 ANSWER 3 OF 4 HCAPLUS COPYRIGHT 2005 ACS on STN

```
2002:637660 HCAPLUS
DN
    137:185501
ED
    Entered STN: 23 Aug 2002
    Preparation of quinazolines as specific inhibitors of type-13 matrix
    metalloprotease
    Andrianjara, Charles; Chantel-Barvian, Nicole; Gaudilliere, Bernard;
    Jacobelli, Henri; Ortwine, Daniel Fred; Patt, William Chester; Pham. Ly;
    Kostlan, Catherine Rose: Wilson, Michael William
    Warner-Lambert Company, USA
S0
    PCT Int. Appl., 264 pp.
    CODEN: PIXXD2
DT
    Patent
    English
LA
IC
    ICM C07D239-96
     ICS C07D401-12; C07D405-12; C07D409-12; C07D405-14; C07D409-14;
          C07D471-04: C07D403-12: C07D403-10: C07D410-10: C07D413-10:
          C07D401-06; A61K031-5025; A61K031-505
    28-16 (Heterocyclic Compounds (More Than One Hetero Atom))
     Section cross-reference(s): 1
FAN.CNT 1
    PATENT NO.
                         KIND
                               -DATE
                                            APPLICATION NO.
                                                                   DATE
                         ----
                                -----
    WO 2002064572
                         A1
                                20020822
                                            WO 2002-EP1979
         W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR.
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
             PL. PT. RO, RU. SD. SE, SG. SI. SK, SL, TJ, TM, TN, TR. TT, TZ.
             UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU,
             TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,
             CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,
             BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
     CA 2437122
                                20020822
                                           CA 2002-2437122
                                                                   20020211
                         AΑ
                         A1
                                20031210
                                            EP 2002-722137
                                                                   20020211
       R: AT. BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE. SI. LT. LV. FI. RO. MK. CY. AL. TR
                                                                   20020211
     EE 200300384
                          Α
                                20031215
                                           EE 2003-384
     JP 2004523546
                          T2
                                20040805
                                           JP 2002-564505
                                                                   20020211
```

```
20020213
     US 2002193377
                                20021219
                                            US 2002-75954
                          A1
                                                                    20030813
     NO 2003003593
                                20030813
                                            NO 2003-3593
                          Α
PRAI US 2001-268661P
                                20010214
     WO 2002-EP1979
                                20020211
CLASS
 PATENT NO.
                 CLASS PATENT FAMILY CLASSIFICATION CODES
 WO 2002064572
                 ICM
                        C07D239-96
                 ICS
                        C07D401-12; C07D405-12; C07D409-12; C07D405-14;
                        C07D409-14; C07D471-04; C07D403-12; C07D403-10;
                        C07D410-10: C07D413-10: C07D401-06: A61K031-5025:
                        A61K031-505
 JP 2004523546
                 FTERM 4C063/AA01: 4C063/AA03: 4C063/BB03: 4C063/BB06:
                        4C063/BB08: 4C063/BB09: 4C063/CC31: 4C063/CC47:
                        4C063/CC58; 4C063/CC81; 4C063/CC92; 4C063/DD12;
                        4C063/DD28; 4C063/DD31; 4C063/EE01; 4C065/AA04;
                        4C065/AAO5; 4C065/BB11; 4C065/CC01; 4C065/DD03;
                        4C065/EE02; 4C065/HH08; 4C065/JJ01; 4C065/KK01;
                        4C065/KK09; 4C065/LL04; 4C065/PP03; 4C065/PP07;
                        4C065/PP12; 4C065/QQ04; 4C065/QQ05; 4C086/AA01;
                        4C086/AA02; 4C086/AA03; 4C086/AA04; 4C086/BC46;
                        4C086/BC62; 4C086/BC71; 4C086/BC73; 4C086/CB09;
                        4C086/GA07; 4C086/GA08; 4C086/GA09; 4C086/GA12;
                        4C086/MA01; 4C086/MA02; 4C086/MA03; 4C086/MA04;
                        4C086/MA05; 4C086/NA14; 4C086/ZA15; 4C086/ZA33;
                        4C086/ZA36; 4C086/ZA45; 4C086/ZA67; 4C086/ZA68;
                        4C086/ZA96; 4C086/ZA97; 4C086/ZB15; 4C086/ZB26;
                        4C086/ZC20; 4C086/ZC41; 4C086/ZC52
     CASREACT 137:185501; MARPAT 137:185501
OS
GI
```

$$(R^2)_{m} - A - (Z^1)_{n} - Z + X^2 \times 1 + X^3 + X^3 = X^3 + X^3 = X^3 + X^3 = X^3 + X^3 = X^3 = X^3 + X^3 = X^3 = X^3 = X^3 + X^3 = X^3$$

Title compds. I [R1 = H. amino. alkyl. alkenyl. alkynyl. alkylamino. aryl. heterocycle, etc.; W = O, S, =N-R'; R' = alkyl. OH, CN; X1-3 = N. C-R6; R6 = H. alkyl. amino. alkylamino. etc.; Y = O. S, NH, N-alkyl; Z = O, S, NR7; R7 = H. alkyl. aryl. aryl. heteroaryl. etc.; n = 1-8; Z1 = alkyl; A = (non)aromatic, 5- or 6-membered monocycle comprising from 0 to 4 heteroatoms selected from N, O, S, etc.; m = 0-7; R2 = alkyl, halo. CN, NO2, SCF3. CF3, OCF3, etc.; R3 = H. alkyl. alkenyl. alkynyl. etc.] were prepared Over 200 synthetic examples were provided. For instance. di-Me 4-aminoisophthalate was reacted with benzylisocyanate and heated to 95-100.degree. overnight to give Me 3-benzyl-2.4-dioxo-1.2.3.4-tetrahydroquinazoline-6-carboxylate which was saponified (dioxaneaq, LiOH, reflux) to give the carboxylic acid. This intermediate was coupled with benzylamine to afford II. Selected examples of I had IC50 = 2.25 - 0.001.mu.M for MMP13 and IC50 > 100.mu.M for MMP1, MMP2, MMP3, MMP7, MMP9.

Truong 10/075954

Page 14

MMP12 and MMP14; II had IC50 = 0.193 .mu.M for MMP13. Compds. I are useful for the treatment of osteoarthritis and rheumatoid arthritis. quinazoline mmp matrix metalloprotease inhibitor prepn IT Antiarteriosclerotics (antiatherosclerotics: preparation of quinazolines as specific inhibitors of type-13 matrix metalloprotease) IT Lung, disease (chronic obstructive; preparation of quinazolines as specific inhibitors of type-13 matrix metalloprotease) TT Heart, disease (failure; preparation of quinazolines as specific inhibitors of type-13 matrix metalloprotease) IT Intestine, disease (inflammatory; preparation of quinazolines as specific inhibitors of type-13 matrix metalloprotease) Eye, disease (macula, senile degeneration; preparation of quinazolines as specific inhibitors of type-13 matrix metalloprotease) Antiarthritics Antiasthmatics Antirheumatic agents Antitumor agents Arthritis Asthma Atherosclerosis Human Multiple sclerosis Neoplasm Osteoarthritis Osteoporosis Periodontium, disease Psoriasis Rheumatoid arthritis (preparation of guinazolines as specific inhibitors of type-13 matrix metalloprotease) IT Multiple sclerosis Osteoporosis (therapeutic agents; preparation of quinazolines as specific inhibitors of type-13 matrix metalloprotease) 449208-02-0P, 3-Benzyl-2.4-dioxo-1.2,3.4-tetrahydroquinazoline-6carboxylic acid (4-pyridylmethyl)amide 449208-14-4P 449208-50-8P. 1-Methyl-2,4-dioxo-1,2,3,4-tetrahydroquinazoline-6-carboxylic acid [benzo[1,3]dioxol-5-ylmethyl]amide 449208-52-0P, Methyl 4-[[6-(4-methoxybenzylcarbamoyl)-1-methyl-2,4-dioxo-1,4-dihydro-2Hquinazolin-3-yl]methyl]benzoate 449208-55-3P, 4-[[6-(4-Methoxybenzylcarbamoyl)-1-methyl-2,4-dioxo-1,4-dihydro-2H-quinazolin-3yl]methyl]benzoic acid 449208-57-5P. 3-Benzyl-2,4-dioxo-1.2.3.4tetrahydroquinazoline-6-carboxylic acid benzyl ester 449208-82-6P 449209-00-1P, [4-[[6-(4-Methoxybenzylcarbamoyl)-1-methyl-2,4-dioxo-1,4dihydro-2H-quinazolin-3-yl]methyl]phenyl]acetic acid 449209-16-9P. Methyl 3-[[6-(4-methoxybenzylcarbamoyl)-1-methyl-2.4-dioxo-1.4-dihydro-2Hquinazolin-3-yl]methyl]benzoate 449209-18-1P, (E)-Methyl 4-[6-(4-methoxybenzylcarbamoyl)-1-methyl-2,4-dioxo-1,4-dihydro-2Hquinazolin-3-yl]but-2-enoate 449209-20-5P. Methyl 5-[[6-(4methoxybenzylcarbamoyl)-1-methyl-2,4-dioxo-1,4-dihydro-2H-quinazolin-3yl]methyl]furan-2-carboxylate 449209-22-7P, Methyl 5-[[6-(4methoxybenzylcarbamoyl)-1-methyl-2,4-dioxo-1,4-dihydro-2H-quinazolin-3yl]methyl]thiophene-2-carboxylate 449209-24-9P 449209-37-4P. Methyl 2-chloro-4-[[6-(4-methoxybenzylcarbamoyl)-1-methyl-2,4-dioxo-1,4-dihydro-

2H-quinazolin-3-yl]methyl]benzoate 449209-43-2P. Methyl

2-methoxy-4-[[6-(4-methoxybenzylcarbamoyl)-1-methyl-2,4-dioxo-1.4-dihydro-2H-quinazolin-3-yl]methyl]benzoate 449209-44-3P. 2-Methoxy-4-[[6-(4-methoxybenzylcarbamoyl)-1-methyl-2,4-dioxo-1,4-dihydro-2H-quinazolin-3-yl]methyl]benzoic acid 449209-45-4P. Methyl 2-hydroxy-4-[[6-(4-methoxybenzylcarbamoyl)-1-methyl-2,4-dioxo-1,4-dihydro-2H-quinazolin-3-yl]methyl]benzoic acid 449209-45-4P. Methyl 2-hydroxy-4-[[6-(4-methoxybenzylcarbamoyl)-1-methyl-2,4-dioxo-1,4-dihydro-2H-quinazolin-3-yl]methyl-2,4-dioxo-1,4-dibydro-2H-quinazolin-3-yl]methyl-2,4-dioxo-1,4-dibydro-2H-quinazolin-3-yl]methyl-2,4-dioxo-1,4-dibydro-2H-quinazolin-3-yl]methyl-2,4-dioxo-1,4-dibydro-2H-quinazolin-3-yl]methyl-2,4-dioxo-1,4-dibydro-2H-quinazolin-3-yl]methyl-2,4-dioxo-1,4-dibydro-2H-quinazolin-3-yl]methyl-2,4-dioxo-1,4-dioxo

Page 15

methoxybenzylcarbamoyl)-1-methyl-2,4-dioxo-1.4-dihydro-2H-quinazolin-3-449209-47-6P, Methyl 2-methyl-4-[[6-(4vllmethvllbenzoate methoxybenzylcarbamoyl)-1-methyl-2,4-dioxo-1,4-dihydro-2H-quinazolin-3-449209-49-8P 449209-52-3P 449209-54-5P, Methyl yl]methyl]benzoate 4-[[6-(3-methoxybenzylcarbamoyl)-1-methyl-2,4-dioxo-1,4-dihydro-2Hquinazolin-3-yl]methyl]benzoate 449209-60-3P, 4-[[1-Methyl-6-((4-(methylsulfanyl)benzyl)carbamoyl)-2,4-dioxo-1,4-dihydro-2H-quinazolin-3yl]methyl]benzoic acid methyl ester 449209-70-5P, 3-(4-Methoxybenzyl)-1methyl-2,4-dioxo-1,2,3,4-tetrahydroquinazoline-6-carboxylic acid ((pyridin-4-yl)methyl)amide 449209-75-0P, Methyl 4-[[1-methyl-2.4-dioxo-6-[(pyridin-4-ylmethyl)carbamoyl]-1,4-dihydro-2H-quinazolin-3yl]methyl]benzoate 449209-89-6P 449209-90-9P 449209-91-0P 449209-95-4P 449209-98-7P, [5-[[6-(4-(Methoxy)benzylcarbamoyl)-1-methyl-2.4-dioxo-1.4-dihydro-2H-quinazolin-3-yl]methyl]pyridin-2-yl]carbamic acid tert-butyl ester 449210-36-0P. 4'-[[6-((4-Methoxybenzyl)carbamoyl)-1methyl-2.4-dioxo-1,4-dihydro-2H-quinazolin-3-yl]methyl]biphenyl-2carboxylic acid methyl ester 449210-88-2P, tert-Butyl 1-[4-[6-(4-methoxybenzylcarbamoyl)-1-methyl-2,4-dioxo-1,4-dihydro-2Hquinazolin-3-yl]methyl]phenyl]cyclopropanecarboxylate 449210-90-6P. 3-Benzyl-6-benzylsulfanyl-1-methyl-1H-quinazoline-2,4-dione 449210-98-4P, 4-[[6-(4-Methoxybenzylcarbamoyl)-1-methyl-2,4-dioxo-1.4dihydro-2H-quinazoline-3-yl]methyl]benzoic acid chloromethyl ester 449210-99-5P 449211-01-2P 474663-15-5P, Ethyl 2-Fluoro-4-[[6-(4methoxybenzylcarbamoyl)-1-methyl-2,4-dioxo-1,4-dihydro-2H-quinazolin-3yl]methyl]benzoate RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study): PREP (Preparation); RACT (Reactant or reagent); USES (Uses) (MMP13 inhibitor; preparation of quinazolines as specific inhibitors of type-13 matrix metalloprotease) 449208-01-9P, 3-Benzyl-2,4-dioxo-1,2,3,4-tetrahydroquinazoline-6carboxylic acid benzylamide 449208-03-1P, 3-Benzyl-2,4-dioxo-1,2,3,4tetrahydroquinazoline-6-carboxylic acid (benzo[1,3]dioxol-5-ylmethyl)amide 449208-04-2P. 3-Benzyl-2.4-dioxo-1.2.3.4-tetrahydroguinazoline-6carboxylic acid (2-thienylmethyl)amide 449208-06-4P. 3-Benzyl-2,4-dioxo-1,2,3,4-tetrahydroquinazoline-6-carboxylic acid (3-pyridylmethyl)amide 449208-07-5P 449208-08-6P 449208-09-7P 449208-10-0P. 3-Benzyl-1-methyl-2,4-dioxo-1,2,3,4-tetrahydroquinazoline-6carboxylic acid (benzo[1,3]dioxol-5-ylmethyl)amide 449208-11-1P. 3-Benzyl-1-methyl-2,4-dioxo-1,2,3,4-tetrahydroquinazoline-6-carboxylic acid benzylamide 449208-12-2P, Methyl 4-[[[1-(3-benzyl-1-methyl-2.4dioxo-1,2,3,4-tetrahydroquinazolin-6-yl)methanoyl]amino]methyl]benzoate 449208-13-3P, 3-Benzyl-1-methyl-2,4-dioxo-1,2,3,4-tetrahydroquinazoline-6carboxylic acid [4-hydroxy-3-methoxybenzyl]amide 449208-15-5P. 3-Benzyl-1-methyl-2,4-dioxo-1,2,3,4-tetrahydroquinazoline-6-carboxylic acid (4-pyridylmethyl)amide 449208-16-6P, 1-Methyl-2.4-dioxo-3-phenethyl-1.2.3.4-tetrahydroquinazoline-6-carboxylic acid [benzo[1.3]dioxol-5ylmethyllamide 449208-20-2P, 3-(4-Methoxybenzyl)-2,4-dioxo-1,2,3,4-

tetrahydroquinazoline-6-carboxylic acid [benzo[1.3]dioxol-5-ylmethyl]amide 449208-22-4P, 3-(4-Methoxybenzyl)-1-methyl-2,4-dioxo-1,2,3,4 $tetrahydroquinazoline-6-carboxylic\ acid\ [benzo[1,3]dioxol-5-ylmethyl] amide$ 449208-23-5P 449208-25-7P, 3-(1-(Naphth-1-yl)ethyl)-2,4-dioxo-1,2,3,4tetrahydroquinazoline-6-carboxylic acid [benzo[1,3]dioxol-5-ylmethyl]amide 449208-26-8P, 2,4-Dioxo-3-((pyridin-4-yl)methyl)-1,2,3,4 $tetra hydroquina zoline-6-carboxylic\ acid\ [benzo[1.3]dioxol-5-ylmethyl] amide$ 449208-32-6P, 2,4-Dioxo-3-(thien-2-ylmethyl)-1,2,3,4-tetrahydroquinazoline-6-carboxylic acid benzylamide 449208-36-0P, 1-Methyl-2.4-dioxo-3-(thien-2-ylmethyl)-1.2.3.4-tetrahydroquinazoline-6-carboxylic acid benzylamide 449208-37-1P, 2.4-Dioxo-3-(thien-2-ylmethyl)-1.2.3.4-tetrahydroquinazoline-6-carboxylic acid [benzo[1,3]dioxol-5-ylmethyl]amide 449208-38-2P. 1-Methyl-2.4-dioxo-3-(thien-2-ylmethyl)-1,2,3.4-tetrahydroquinazoline-6carboxylic acid [benzo[1.3]dioxol-5-ylmethyl]amide 449208-39-3P. 3-(4-Chlorobenzyl)-2,4-dioxo-1,2,3,4-tetrahydroquinazoline-6-carboxylic acid [benzo[1,3]dioxol-5-ylmethyl]amide 449208-40-6P.

```
3-(4-Chlorobenzyl)-1-methyl-2.4-dioxo-1.2.3.4-tetrahydroguinazoline-6-
carboxylic acid [benzo[1,3]dioxol-5-ylmethyl]amide 449208-41-7P.
1,3-Dimethyl-2,4-dioxo-1,2,3,4-tetrahydroquinazoline-6-carboxylic acid
[benzo[1.3]dioxol-5-ylmethyl]amide 449208-42-8P, 3-((Benzo[1.3]dioxol-5-
yl)methyl)-2,4-dioxo-1,2,3,4-tetrahydroquinazoline-6-carboxylic acid
[benzo[1,3]dioxol-5-ylmethyl]amide 449208-46-2P, 3-((Benzo[1,3]dioxol-5-
yl)methyl)-1-methyl-2.4-dioxo-1,2,3,4-tetrahydroquinazoline-6-carboxylic
acid [benzo[1,3]dioxol-5-ylmethyl]amide 449208-47-3P.
3-Benzyl-1-ethyl-2.4-dioxo-1.2.3.4-tetrahydroguinazoline-6-carboxylic acid
[benzo[1,3]dioxol-5-ylmethyl]amide 449208-48-4P. 3-Benzyl-1-
cyclopropylmethyl-2.4-dioxo-1,2,3,4-tetrahydroquinazoline-6-carboxylic
acid [benzo[1,3]dioxol-5-ylmethyl]amide 449208-49-5P.
3-Benzyl-1-isobutyl-2,4-dioxo-1,2,3,4-tetrahydroquinazoline-6-carboxylic
acid [benzo[1.3]dioxol-5-ylmethyl]amide 449208-56-4P.
1-Methyl-2.4-dioxo-3-((E)-3-phenylpropenyl)-1.2.3.4-tetrahydroquinazoline-
6-carboxylic acid [benzo[1.3]dioxol-5-ylmethyl]amide 449208-58-6P.
3-Benzyl-1-methyl-2,4-dioxo-1,2,3,4-tetrahydroquinazoline-6-carboxylic
acid benzyl ester 449208-59-7P, 3-Benzyl-2.4-dioxo-1.2.3.4-
tetrahydroquinazoline-6-carboxylic acid 4-pyridylmethyl ester
449208-60-0P 449208-61-1P, 3-Benzyl-2,4-dioxo-1,2,3,4-
tetrahydroquinazoline-6-carboxylic acid [Benzo[1,3]dioxol-5-yl]methyl
      449208-62-2P, 3-Benzyl-1-methyl-2,4-dioxo-1,2,3,4-
tetrahydroquinazoline-6-carboxylic acid [Benzo[1,3]dioxol-5-yl]methyl
ester 449208-63-3P, 1-Benzyl-2,4-dioxo-3-((pyridin-4-yl)methyl)-1,2,3,4-
tetrahydroquinazoline-6-carboxylic acid benzyl ester 449208-64-4P.
2,4-Dioxo-3-(thien-2-ylmethyl)-1,2,3,4-tetrahydroquinazoline-6-carboxylic
acid 4-Pyridylmethyl ester 449208-65-5P, 3-((Benzo[1,3]dioxol-5-
yl)methyl)-2,4-dioxo-1,2,3,4-tetrahydroquinazoline-6-carboxylic acid
4-Pyridylmethyl ester 449208-66-6P, Benzyl 3-benzyl-2,4-dioxo-1,2,3,4-
tetrahydropyrido[2,3-d]pyrimidine-6-carboxylate 449208-67-7P.
3-Benzyl-6-methyl-1H-pyrido[2.3-d]pyrimidine-2,4-dione 449208-69-9P.
4-Pyridylmethyl 3-benzyl-2,4-dioxo-1,2,3,4-tetrahydropyrido[2,3-
d]pyrimidine-6-carboxylate 449208-70-2P, 3-Benzyl-4-oxo-2-thioxo-1,2,3,4-
tetrahydroguinazoline-6-carboxylic acid [benzo[1,3]dioxol-5-ylmethyl]amide
449208-71-3P, 4-[[6-(4-Hydroxybenzylcarbamoyl)-1-methyl-2,4-dioxo-1,4-
dihydro-2H-quinazolin-3-yl]methyl]benzoic acid 449208-72-4P
449208-73-5P
              449208-74-6P
                            449208-75-7P 449208-76-8P
                                                          449208-77-9P
                                            449208-81-5P
                                                          449208-83-7P
449208-78-0P
              449208-79-1P
                             449208-80-4P
449208-84-8P
                             449208-87-1P
                                            449208-88-2P
                                                          449208-89-3P
              449208-85-9P
449208-90-6P
              449208-91-7P 449208-92-8P
                                            449208-93-9P, Ethyl
[6-(4-methoxybenzylcarbamoyl)-1-methyl-2,4-dioxo-1,4-dihydro-2H-quinazolin-
3-y1]acetate 449208-94-0P 449208-95-1P, Methyl 3-[6-(4-
methoxybenzylcarbamoyl)-1-methyl-2,4-dioxo-1,4-dihydro-2H-quinazolin-3-
yl]propionate 449208-96-2P, 3-[6-(4-Methoxybenzylcarbamoyl)-1-methyl-2,4-
dioxo-1,4-dihydro-2H-quinazolin-3-yl]propionic acid 449208-97-3P
449208-98-4P, 4-[6-(4-Methoxybenzylcarbamoyl)-1-methyl-2,4-dioxo-1,4-
dihydro-2H-quinazolin-3-yl]butyric acid 449208-99-5P. Methyl
[4-[[6-(4-methoxybenzylcarbamoyl)-1-methyl-2,4-dioxo-1,4-dihydro-2H-
quinazolin-3-yl]methyl]phenyl]acetate 449209-01-2P 449209-02-3P
449209-04-5P 449209-06-7P 449209-07-8P
                                            449209-09-0P
                                                          449209-13-6P
449209-14-7P
              449209-17-0P, 3-[[6-(4-Methoxybenzylcarbamoyl)-1-methyl-2.4-
dioxo-1,4-dihydro-2H-quinazolin-3-yl]methyl]benzoic acid 449209-19-2P.
4-[6-(4-Methoxybenzylcarbamoyl)-1-methyl-2,4-dioxo-1,4-dihydro-2H-
quinazolin-3-yl]but-2-enoic acid 449209-21-6P, 5-[[6-(4-
Methoxybenzylcarbamoyl)-1-methyl-2.4-dioxo-1,4-dihydro-2H-quinazolin-3-
yl]methyl]furan-2-carboxylic acid 449209-23-8P. 5-[[6-(4-
Methoxybenzylcarbamoyl)-1-methyl-2,4-dioxo-1,4-dihydro-2H-quinazolin-3-
yl]methyl]thiophene-2-carboxylic acid 449209-25-0P 449209-26-1P
449209-27-2P
              449209-28-3P
                            449209-29-4P
                                            449209-30-7P
                                                          449209-31-8P
449209-32-9P
              449209-33-0P
                            449209-34-1P
                                            449209-36-3P
                                                          449209-39-6P.
2-Chloro-4-[[6-(4-methoxybenzylcarbamoyl)-1-methyl-2.4-dioxo-1.4-dihydro-
2H-quinazolin-3-yl]methyl]benzoic acid 449209-40-9P 449209-41-0P
449209-46-5P. 2-Hydroxy-4-[[6-(4-methoxybenzylcarbamoyl)-1-methyl-2.4-
dioxo-1.4-dihydro-2H-quinazolin-3-yl]methyl]benzoic acid 449209-48-7P.
```

```
2-Methyl-4-[[6-(4-methoxybenzylcarbamoyl)-1-methyl-2,4-dioxo-1,4-dihydro-
2H-quinazolin-3-yl]methyl]benzoic acid 449209-53-4P 449209-59-0P.
4-[[6-(3-Methoxybenzylcarbamoyl)-1-methyl-2,4-dioxo-1,4-dihydro-2H-
quinazolin-3-yl]methyl]benzoic acid 449209-61-4P, 4-[[1-Methyl-6-(4-
methylsulfanylbenzylcarbamoyl)-2,4-dioxo-1,4-dihydro-2H-quinazolin-3-
yl]methyl]benzoic acid 449209-62-5P, 4-[[1-Methyl-2,4-dioxo-6-(4-
(trifluoromethoxy)benzylcarbamoyl)-1,4-dihydro-2H-quinazolin-3-
yl]methyl]benzoic acid methyl ester 449209-63-6P. Methyl
4-[[6-(4-fluorobenzylcarbamoyl)-1-methyl-2,4-dioxo-1,4-dihydro-2H-
quinazolin-3-yl]methyl]benzoate 449209-64-7P, 4-[[6-(4-
Fluorobenzylcarbamoyl)-1-methyl-2,4-dioxo-1,4-dihydro-2H-quinazolin-3-
y1]methy1]benzoic acid 449209-65-8P. Methy1 4-[[6-[(benzofurazan-5-
ylmethyl)carbamoyl]-1-methyl-2.4-dioxo-1.4-dihydro-2H-quinazolin-3-
yl]methyl]benzoate 449209-66-9P, 4-[[6-[(Benzofurazan-5-
ylmethyl)carbamoyl]-1-methyl-2,4-dioxo-1,4-dihydro-2H-quinazolin-3-
yl]methyl]benzoic acid 449209-67-0P, Methyl 4-[[6-(4-
methoxybenzylcarbamoyl)-2,4-dioxo-1,4-dihydro-2H-quinazolin-3-
yl]methyl]benzoate 449209-68-1P, Methyl 4-[[1-ethyl-6-(4-
methoxybenzylcarbamoyl)-2,4-dioxo-1,4-dihydro-2H-quinazolin-3-
y1]methy1]benzoate 449209-69-2P, 4-[[1-Ethy1-6-(4-
methoxybenzylcarbamoyl)-2.4-dioxo-1,4-dihydro-2H-quinazolin-3-
yl]methyl]benzoic acid 449209-71-6P, 3-(4-Hydroxybenzyl)-1-methyl-2.4-
dioxo-1.2.3.4-tetrahydroguinazoline-6-carboxylic acid ((pyridin-4-
v1)methy1)amide 449209-72-7P, 3-(4-Cyanobenzy1)-1-methy1-2,4-dioxo-
1,2,3,4-tetrahydroquinazoline-6-carboxylic acid ((pyridin-4-
yl)methyl)amide 449209-74-9P, 1-Methyl-2,4-dioxo-3-(3-(pyridin-4-
yl)propenyl)-1,2,3,4-tetrahydroguinazoline-6-carboxylic acid
((pyridin-4-yl)methyl)amide 449209-76-1P, 4-[[1-Methyl-2,4-dioxo-6-
[(pyridin-4-ylmethyl)carbamoyl]-1,4-dihydro-2H-quinazolin-3-
yl]methyl]benzoic acid hydrochloride 449209-77-2P, Methyl [4-[[1-methyl-2,4-dioxo-6-[(pyridin-4-ylmethyl)carbamoyl]-1,4-dihydro-2H-
quinazolin-3-yl]methyl]phenyl]acetate 449209-78-3P, [4-[[1-Methyl-2.4-
dioxo-6-[(pyridin-4-ylmethyl)carbamoyl]-1,4-dihydro-2H-quinazolin-3-
yl]methyl]phenyl]acetic acid hydrochloride 449209-79-4P
449209-81-8P, Methyl [6-[(1,3-Benzodioxol-5-ylmethyl)carbamoyl]-3-benzyl-
2.4-dioxo-1.4-dihydro-2H-quinazolin-1-yl]acetate 449209-82-9P.
[6-[(1.3-Benzodioxol-5-ylmethyl)carbamoyl]-3-benzyl-2.4-dioxo-3.4-dihydro-
2H-quinazolin-1-vllacetic acid 449209-83-0P. Methyl 4-[[6-[(1,3-
benzodioxol-5-ylmethyl)carbamoyl]-1-methyl-2,4-dioxo-1,4-dihydro-2H-
quinazolin-3-yl]methyl]benzoate 449209-84-1P, 4-[[6-[(1.3-Benzodioxol-5-
ylmethyl)carbamoyl]-1-methyl-2,4-dioxo-1,4-dihydro-2H-quinazolin-3-
yl]methyl]benzoic acid 449209-85-2P, 3-Benzyl-1-methyl-2,4-dioxo-1,2,3,4-
tetrahydroquinazoline-6-carboxylic acid (4-(sulfamoyl)benzyl)amide
449209-86-3P. 3-Benzyl-1-methyl-2,4-dioxo-1,2,3,4-tetrahydroquinazoline-6-
carboxylic acid [3-(pyridin-4-ylsulfanyl)propyl]amide
                                                       449209-87-4P,
3-Benzyl-1-methyl-2,4-dioxo-1,2,3,4-tetrahydroquinazoline-6-carboxylic
acid (4-morpholin-4-ylbutyl)amide 449209-88-5P
                                                  449209-92-1P,
3-Benzyl-1-methyl-2,4-dioxo-1,2,3,4-tetrahydroquinazoline-6-carboxylic
acid (4-((dimethylcarbamovl)methoxy)benzyl)amide 449209-93-2P
449209-94-3P
             449209-96-5P, 3-Benzyl-1-methyl-2.4-dioxo-1.2.3.4-
tetrahydroquinazoline-6-carboxylic acid (4-(dimethylcarbamoyl)benzyl)amide
449209-97-6P 449209-99-8P 449210-00-8P, 1,3-Dimethyl-2,4-dioxo-1,2,3,4-
tetrahydropyrido[2.3-d]pyrimidine-6-carboxylic acid [benzo[1.3]dioxol-5-
ylmethyl]amide 449210-01-9P, 1.3-Dimethyl-2.4-dioxo-1.2.3.4-
tetrahydropyrido[3,4-d]pyrimidine-6-carboxylic acid [benzo[1.3]dioxol-5-
ylmethyl]amide 449210-03-1P, 3-Benzyl-1-methyl-2,4-dioxo-1,2,3,4-
tetrahydropyrido[2,3-d]pyrimidine-6-carboxylic acid [benzo[1,3]dioxol-5-
ylmethyl]amide 449210-07-5P, 4-[[6-(4-Methoxybenzylcarbamoyl)-1-
methyl-2,4-dioxo-1,4-dihydro-2H-pyrido[2,3-d]pyrimidin-3-yl]methyl]benzoic
acid 449210-11-1P 449210-12-2P 449210-13-3P.
3-Benzyl-1-methyl-2,4-dioxo-1,2,3,4-tetrahydropyrido[3,4-d]pyrimidine-6-
carboxylic acid [benzo[1,3]dioxol-5-ylmethyl]amide 449210-20-2P.
Methyl 4-[[6-(4-Methoxybenzylcarbamoyl)-1-methyl-2,4-dioxo-1,4-dihydro-2H-
pyrido[3,4-d]pyrimidin-3-yl]methyl]benzoate 449210-23-5P, tert-Butyl
```

```
4-[[6-(4-methoxybenzylcarbamoyl)-1-methyl-2.4-dioxo-1.4-dihydro-2H-
pyrido[3,4-d]pyrimidin-3-yl]methyl]benzoate 449210-24-6P.
4-[[6-(3-Methoxybenzylcarbamoyl)-1-methyl-2,4-dioxo-1,4-dihydro-2H-
pyrido[3,4-d]pyrimidin-3-yl]methyl]benzoic acid 449210-27-9P
449210-28-0P, 3-Benzyl-1-methyl-6-(3-phenylpropionyl)-1H-quinazoline-2.4-
dione 449210-29-1P 449210-30-4P 449210-31-5P. 3-Benzyl-1-methyl-6-[2-
(pyridin-4-ylsulfanyl)acetyl]-1H-quinazoline-2,4-dione 449210-32-6P
449210-33-7P 449210-34-8P 449210-37-1P, 4'-[[6-(4-
Methoxybenzylcarbamoyl)-1-methyl-2.4-dioxo-1.4-dihydro-2H-quinazolin-3-
yl]methyl]biphenyl-2-carboxylic acid 449210-39-3P. 2-Fluoro-4-[[6-(4-
methoxybenzylcarbamoyl)-1-methyl-2,4-dioxo-1,4-dihydro-2H-quinazolin-3-
yl]methyl]benzoic acid 449210-40-6P, 2-Methoxy-4-[[6-(4-
methoxybenzylcarbamoyl)-1-methyl-2,4-dioxo-1,4-dihydro-2H-quinazolin-3-
yl]methyl]benzoic acid 2-dimethylaminoethyl ester 449210-41-7P.
4-[[6-(4-Methoxybenzylcarbamoyl)-1-methyl-2,4-dioxo-1,4-dihydro-2H-
quinazolin-3-yl]methyl]-2-methylbenzoic acid 2-dimethylaminoethyl ester
449210-42-8P 449210-43-9P, [4-[6-(4-Methoxybenzylcarbamoyl)-1-methyl-2.4-
dioxo-1.4-dihydro-2H-quinazolin-3-yl]phenyl]acetic acid
1-Methy]-3-(1-(naphthalen-1-yl)ethyl)-2,4-dioxo-1,2,3,4-
tetrahydroquinazoline-6-carboxylic\ acid\ [benzo[1.3] dioxol-5-ylmethyl] amide
449210-47-3P. 4-[[6-(4-Methoxybenzylcarbamoyl)-1-methyl-2.4-dioxo-
1,4-dihydro-2H-pyrido[3,4-d]pyrimidin-3-yl]methyl]benzoic acid
449210-49-5P, 3-(3-Fluorobenzyl)-1-methyl-2,4-dioxo-1,2,3,4-
tetrahydroquinazoline-6-carboxylic acid ((pyridin-4-yl)methyl)amide
449210-51-9P. 3-(3-Fluorobenzyl)-1-methyl-2.4-dioxo-1.2.3.4-
tetrahydroguinazoline-6-carboxylic acid ((2-methoxypyridin-4-
yl)methyl)amide 449210-52-0P, 3-(3-Fluorobenzyl)-1-methyl-2.4-dioxo-
1,2,3,4-tetrahydroquinazoline-6-carboxylic acid ((pyridin-3-
yl)methyl)amide 449210-53-1P 449210-54-2P 449210-55-3P.
1-Ethyl-3-(3-fluorobenzyl)-2,4-dioxo-1,2,3,4-tetrahydroquinazoline-6-
carboxylic acid ((pyridin-4-yl)methyl)amide 449210-56-4P.
1-Ethyl-3-(3-fluorobenzyl)-2.4-dioxo-1,2,3,4-tetrahydroquinazoline-6-
carboxylic acid ((pyridin-3-yl)methyl)amide 449210-57-5P 449210-61-1P.
3-(4-Bromobenzyl)-1-methyl-2.4-dioxo-1,2,3,4-tetrahydroquinazoline-6-
carboxylic acid ((2-methoxypyridin-4-yl)methyl)amide 449210-62-2P.
3-(3,4-Difluorobenzyl)-1-methyl-2,4-dioxo-1,2,3,4-tetrahydroquinazoline-6-
carboxylic acid (pyridin-3-ylmethyl)amide 449210-66-6P.
3-(3.4-Difluorobenzyl)-1-methyl-2.4-dioxo-1.2.3.4-tetrahydroguinazoline-6-
carboxylic acid (pyridin-4-ylmethyl)amide 449210-67-7P 449210-68-8P.
3-(3-Chloro-4-fluorobenzyl)-1-methyl-2,4-dioxo-1,2,3,4-
tetrahydroquinazoline-6-carboxylic acid ((pyridin-4-yl)methyl)amide
449210-72-4P 449210-73-5P 449210-74-6P 449210-75-7P 449210-76-8P.
3-(4-Chlorobenzyl)-1-methyl-2,4-dioxo-1,2,3,4-tetrahydroquinazoline-6-
carboxylic acid ((pyridin-4-yl)methyl)amide 449210-78-0P.
3-(4-Fluorobenzyl)-1-methyl-2,4-dioxo-1,2,3,4-tetrahydroquinazoline-6-
carboxylic acid ((pyridin-4-yl)methyl)amide 449210-79-1P.
3-(4-Fluorobenzyl)-1-methyl-2,4-dioxo-1,2,3,4-tetrahydroquinazoline-6-
carboxylic acid ((pyridin-3-yl)methyl)amide 449210-81-5P.
3-(4-Chlorobenzyl)-1-methyl-2,4-dioxo-1,2,3,4-tetrahydroguinazoline-6-
carboxylic acid ((pyridin-3-yl)methyl)amide
                                             449210-82-6P
                                                            449210-84-8P
449210-85-9P. 3-(4-Fluorobenzyl)-1-methyl-2,4-dioxo-1,2,3,4-
tetrahydroquinazoline-6-carboxylic acid ((2-methoxypyridin-4-
yl)methyl)amide 449210-87-1P, 3-(4-Chlorobenzyl)-1-methyl-2,4-dioxo-
1.2.3.4-tetrahydroguinazoline-6-carboxylic acid ((2-methoxypyridin-4-
yl)methyl)amide 449210-89-3P, 1-[4-[[6-(4-Methoxybenzylcarbamoyl)-1-
methyl-2,4-dioxo-1,4-dihydro-2H-quinazolin-3-yl]methyl]phenyl]cyclopropane
carboxylic acid 449210-92-8P, 3-Benzyl-1-methyl-6-
((phenylmethyl)sulfinyl)-1H-quinazoline-2.4-dione 449210-93-9P.
3-Benzyl-1-methyl-6-((phenylmethyl)sulfonyl)-1H-quinazoline-2,4-dione
449210-94-0P 449210-95-1P. 4-[[6-(4-Methoxybenzylcarbamoyl)-1-methyl-2.4-
dioxo-1,4-dihydro-2H-quinazoline-3-yl]methyl]benzoic acid
3-(dimethylamino)-2,2-dimethylpropyl ester 449210-96-2P.
4-[[6-((4-Methoxybenzyl)carbamoyl)-1-methyl-2.4-dioxo-1.4-dihydro-2H-
quinazoline-3-yl]methyl]benzoic acid 2-(dimethylamino)-2-methylpropyl
```

449210-97-3P, 4-[[6-(4-Methoxybenzylcarbamoyl)-1-methyl-2,4-dioxo-

1.4-dihydro-2H-quinazoline-3-yl]methyl]benzoic acid 2-dimethylaminoethyl

```
449211-00-1P 449211-04-5P 449211-08-9P 449211-12-5P.
 4-[[6-((3-Methoxybenzylcarbamoyl)methyl)-2,4-dioxo-1,4-dihydro-2H-
 quinazolin-3-yl]methyl]benzoic acid methyl ester 449211-14-7P,
 4-[[1-Ethyl-2,4-dioxo-6-((4-(trifluoromethoxy)benzyl)carbamoyl)-1.4-
 dihydro-2H-quinazolin-3-yl]methyl]benzoic acid methyl ester
 449211-16-9P, 4-[[1-Methyl-2,4-dioxo-6-[(pyridin-4-ylmethyl)carbamoyl]-1,4-
 dihydro-2H-quinazolin-3-yl]methyl]benzoic acid 449211-18-1P.
 [4-[[1-Methyl-2,4-dioxo-6-[(pyridin-4-ylmethyl)carbamoyl]-1,4-dihydro-2H-
 quinazolin-3-yl]methyl]phenyl]acetic acid
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
 (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
 (Uses)
    (MMP13 inhibitor; preparation of quinazolines as specific inhibitors of
    type-13 matrix metalloprotease)
4315-09-7P, 4-Nitroisophthalic acid
                                       23965-06-2P, 3-Benzyl-6-bromo-1H-
 quinazoline-2.4-dione 33857-88-4P
                                      63746-12-3P, Dimethyl
 4-aminoisophthalate 69048-70-0P. Dimethyl 4-nitroisophthalate
 69209-73-0P 151979-21-4P, 5-Iodo-2-((methyl)amino)benzoic acid
 177913-48-3P. Dimethyl 4-amino-1-hydroxycyclohexa-3.5-diene-1.3-
 dicarboxylate 184681-83-2P, 1,3-Dimethyl-2,4-dioxo-1,2,3,4-
 tetrahydropyrido[2,3-d]pyrimidine-6-carboxylic acid 209604-61-5P.
 3-Benzyl-2.4-dioxo-1.2.3.4-tetrahydroquinazoline-6-carboxylic acid methyl
 ester 221540-53-0P, 3-(4-Methoxybenzyl)-2.4-dioxo-1.2.3.4-
 tetrahydroquinazoline-6-carboxylic acid methyl ester 342644-48-8P.
 3-Benzyl-1-methyl-2,4-dioxo-1,2,3,4-tetrahydropyrido[2,3-d]pyrimidine-6-
 carboxylic acid ethyl ester 449207-91-4P, 3-Benzyl-2,4-dioxo-1,2,3,4-
 tetrahydroguinazoline-6-carboxylic acid 449207-92-5P 449207-93-6P.
 3-Benzyl-2,4-dioxo-1,2,3,4-tetrahydroguinazoline-6-carbonitrile
 449207-94-7P, 3-Benzyl-1-methyl-2,4-dioxo-1,2,3,4-tetrahydroquinazoline-6-
 carboxylic acid 449207-95-8P, 3-Benzyl-1-methyl-2,4-dioxo-1,2,3,4-
 tetrahydroquinazoline-6-carboxylic acid methyl ester 449207-96-9P.
 1-Methyl-3-(3-fluorobenzyl)-2.4-dioxo-1.2.3.4-tetrahydroquinazoline-6-
 carboxylic acid 449207-97-0P. 3-(3-Fluorobenzyl)-2.4-dioxo-1.2.3.4-
 tetrahydroquinazoline-6-carboxylic acid methyl ester 449207-98-1P.
 1-Methyl-3-(3-fluorobenzyl)-2,4-dioxo-1,2,3,4-tetrahydroquinazoline-6-
 carboxylic acid methyl ester 449207-99-2P, 1-Ethyl-3-(3-fluorobenzyl)-
 2.4-dioxo-1.2.3.4-tetrahydroquinazoline-6-carboxylic acid 449208-00-8P,
 1-Ethyl-3-(3-fluorobenzyl)-2,4-dioxo-1,2,3,4-tetrahydroquinazoline-6-
 carboxylic acid methyl ester 449208-17-7P, 2,4-Dioxo-3-phenethyl-1,2,3,4-
 tetrahydroquinazoline-6-carboxylic acid methyl ester 449208-18-8P.
 2.4-Dioxo-3-phenethyl-1.2.3.4-tetrahydroquinazoline-6-carboxylic acid
 449208-19-9P, 2.4-Dioxo-3-phenethyl-1,2.3.4-tetrahydroquinazoline-6-
 carboxylic acid [benzo[1,3]dioxol-5-ylmethyl]amide 449208-21-3P.
 3-(4-Methoxybenzyl)-2,4-dioxo-1,2,3,4-tetrahydroquinazoline-6-carboxylic
 acid 449208-24-6P, 3-(4-Methoxybenzyl)-2,4-dioxo-1,2,3.4-
 tetrahydroquinazoline-6-carboxylic acid (4-methoxybenzyl)amide
 449208-27-9P, Dimethyl 4-(N'-((pyridin-4-yl)methyl)ureido)isophthalate
 449208-29-1P. 2.4-Dioxo-3-((pyridin-4-yl)methyl)-1.2.3.4-
 tetrahydroquinazoline-6-carboxylic acid methyl ester 449208-31-5P.
 2.4-Dioxo-3-((pyridin-4-yl)methyl)-1.2.3.4-tetrahydroquinazoline-6-
 carboxylic acid 449208-33-7P 449208-34-8P, 2.4-Dioxo-3-(thien-2-
 vlmethyl)-1.2.3.4-tetrahydroguinazoline-6-carboxylic acid methyl ester
 449208-35-9P, 2.4-Dioxo-3-(thien-2-ylmethyl)-1,2,3,4-tetrahydroquinazoline-
 6-carboxylic acid 449208-43-9P 449208-44-0P, 3-((Benzo[1,3]dioxol-5-
 yl)methyl)-2.4-dioxo-1.2.3.4-tetrahydroquinazoline-6-carboxylic acid
 methyl ester 449208-45-1P. 3-((Benzo[1,3]dioxol-5-yl)methyl)-2,4-dioxo-
 1.2.3.4-tetrahydroquinazoline-6-carboxylic acid 449208-51-9P,
 1-Methyl-2,4-dioxo-1.2.3.4-tetrahydroquinazoline-6-carboxylic acid methyl
 ester 449208-53-1P 449208-68-8P, 3-Benzyl-2,4-dioxo-1,2,3,4-
 tetrahydropyrido[2,3-d]pyrimidine-6-carboxylic acid 449209-10-3P.
 3-(4-Chlorosulfonylbenzyl)-1-methyl-2,4-dioxo-1,2,3,4-
 tetrahydroquinazoline-6-carboxylic acid methyl ester 449209-11-4P.
```

```
3-(4-Dimethylsulfamoylbenzyl)-1-methyl-2.4-dioxo-1,2,3,4-
tetrahydroquinazoline-6-carboxylic acid methyl ester 449209-12-5P.
3-(4-Dimethylsulfamoylbenzyl)-1-methyl-2,4-dioxo-1.2,3,4-
tetrahydroguinazoline-6-carboxylic acid 449209-15-8P.
1-Methyl-3-(4-methylsulfamoylbenzyl)-2.4-dioxo-1.2.3.4-
tetrahydroquinazoline-6-carboxylic acid methyl ester 449209-50-1P.
2,4-Dioxo-1-methyl-3-(pyridin-4-ylmethyl)-1,2,3,4-tetrahydroquinazoline-6-
carboxylic acid methyl ester 449209-51-2P, 2,4-Dioxo-1-methyl-3-
(pyridine-4-ylmethyl)-1,2,3,4-tetrahydroquinazoline-6-carboxylic acid
449209-55-6P, 3-(4-Methoxycarbonylbenzyl)-2,4-dioxo-1,2,3,4-
tetrahydroquinazoline-6-carboxylic acid benzyl ester 449209-57-8P.
3-(4-Methoxycarbonylbenzyl)-1-methyl-2.4-dioxo-1.2.3,4-
tetrahydroquinazoline-6-carboxylic acid benzyl ester 449209-58-9P.
3-(4-Methoxycarbonylbenzyl)-1-methyl-2,4-dioxo-1,2,3.4-
tetrahydroquinazoline-6-carboxylic acid 449209-73-8P.
1-Methyl-2,4-dioxo-1,2,3,4-tetrahydroquinazoline-6-carboxylic acid
(pyridin-4-ylmethyl)amide 449210-02-0P, 1.3-Dimethyl-2.4-dioxo-1.2.3.4-
tetrahydropyrido[3,4-d]pyrimidine-6-carboxylic acid 449210-04-2P
449210-05-3P 449210-06-4P. 3-Benzyl-1-methyl-2,4-dioxo-1,2,3,4-
tetrahydropyrido[2,3-d]pyrimidine-6-carboxylic acid 449210-08-6P.
1-Methyl-2,4-dioxo-1,2,3,4-tetrahydropyrido[2.3-d]pyrimidine-6-carboxylic
acid 449210-09-7P 449210-10-0P, Methyl 4-[[6-(4-
Methoxybenzylcarbamoyl)-1-methyl-2,4-dioxo-1,4-dihydro-2H-pyrido[2.3-
d]pyrimidin-3-yl]methyl]benzoate 449210-14-4P, 1-Benzyl-2,6-dioxo-
1,2,3,6-tetrahydropyrimidine-4-carboxaldehyde 449210-15-5P
449210-16-6P 449210-17-7P 449210-18-8P, 3-Benzyl-1-methyl-2,4-dioxo-
1.2.3.4-tetrahydropyrido[3,4-d]pyrimidine-6-carboxylic acid methyl ester
449210-19-9P, 3-Benzyl-1-methyl-2,4-dioxo-1,2,3,4-tetrahydropyrido[3,4-
d]pyrimidine-6-carboxylic acid 449210-21-3P, 1-Methyl-2,4-dioxo-1.2,3,4-
tetrahydropyrido[3,4-d]pyrimidine-6-carboxylic acid 449210-22-4P
449210-25-7P 449210-26-8P, tert-Butyl 4-[[6-(3-Methoxybenzylcarbamoyl)-1-
methyl-2,4-dioxo-1,4-dihydro-2H-pyrido[3,4-d]pyrimidin-3-
yl]methyl]benzoate 449210-58-6P. 3-(4-Bromobenzyl)-2.4-dioxo-1,2,3.4-
tetrahydroquinazoline-6-carboxylic acid methyl ester 449210-59-7P.
1-Methyl-3-(4-bromobenzyl)-2,4-dioxo-1,2,3,4-tetrahydroquinazoline-6-
carboxylic acid methyl ester 449210-60-0P, 1-Methyl-3-(4-bromobenzyl)-
2.4-dioxo-1.2.3.4-tetrahydroquinazoline-6-carboxylic acid 449210-63-3P.
3-(3,4-Difluorobenzyl)-2,4-dioxo-1,2,3,4-tetrahydroquinazoline-6-
carboxylic acid methyl ester 449210-64-4P, 1-Methyl-3-(3.4-
difluorobenzyl)-2,4-dioxo-1,2,3,4-tetrahydroquinazoline-6-carboxylic acid
methyl ester 449210-65-5P, 1-Methyl-3-(3,4-difluorobenzyl)-2,4-dioxo-
1,2,3,4-tetrahydroquinazoline-6-carboxylic acid 449210-69-9P.
3-(3-Chloro-4-fluorobenzyl)-2.4-dioxo-1.2.3.4-tetrahydroquinazoline-6-
carboxylic acid methyl ester 449210-70-2P, 1-Methyl-3-(3-chloro-4-
fluorobenzyl)-2.4-dioxo-1,2,3,4-tetrahydroquinazoline-6-carboxylic acid
methyl ester 449210-71-3P, 1-Methyl-3-(3-chloro-4-fluorobenzyl)-2,4-
dioxo-1.2.3.4-tetrahydroquinazoline-6-carboxylic acid 449210-77-9P.
1-Methyl-2.4-dioxo-1,2,3,4-tetrahydroquinazoline-6-carboxylic acid
(pyridazin-4-ylmethyl)amide 449210-80-4P, 1-Methyl-2,4-dioxo-1.2.3.4-
tetrahydroquinazoline-6-carboxylic acid (pyridin-3-ylmethyl)amide
449210-83-7P 449210-86-0P, 1-Methyl-2,4-dioxo-1,2,3,4-
tetrahydroquinazoline-6-carboxylic acid ((2-methoxypyridin-4-
yl)methyl)amide 449210-91-7P, 3-Benzyl-6-iodo-1-methyl-1H-quinazoline-
2.4-dione
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
   (intermediate: preparation of quinazolines as specific inhibitors of type-13
   matrix metalloprotease)
9001-12-1, MMP-1 9004-06-2, MMP-12 79955-99-0, MMP 3 141256-52-2.
MMP 7 146480-35-5, MMP-2 146480-36-6, MMP-9 161384-17-4, MMP-14
175449-82-8, MMP-13
RL: BSU (Biological study, unclassified): BIOL (Biological study)
   (preparation of guinazolines as specific inhibitors of type-13 matrix
   metalloprotease)
```

IT 78-73-9, Choline bicarbonate 78-77-3, Isobutyl bromide 79-07-2. 2-Chloroacetamide 96-32-2, Methyl bromoacetate 96-33-3, Methyl acrylate 100-11-8, 4-Nitrobenzyl bromide 100-44-7, Benzyl chloride. reactions 100-46-9, Benzylamine, reactions 100-51-6, Benzyl alcohol. 104-84-7, 4-Methylbenzylamine 104-86-9, 4-Chlorobenzylamine reactions 105-36-2, Ethyl bromoacetate 105-39-5. Ethyl 2-chloroacetate 106-95-6. Allyl bromide, reactions 106-96-7, Prop-2-ynyl bromide 108-00-9. N.N-Dimethylethylene diamine 108-01-0, 2-(Dimethylamino)ethanol 119-68-6, N-Methylanthranilic acid 138-39-6, 4-(Aminomethyl)benzenesulfonamide 140-75-0, 4-Fluorobenzylamine 140-88-5. Ethyl acrylate 332-48-9, 2-(4-Fluorophenoxy)ethyl bromide 351-52-0, 4-Chloromethyl-2-fluoro-1-methoxybenzene 459-46-1 495-76-1, Piperonyl alcohol 540-51-2, 2-Bromoethanol 586-95-8, 4-Pyridylcarbinol 593-71-5, Chloroiodomethane 622-78-6, Benzyl isothiocyanate 622-95-7, 4-Chlorobenzyl bromide 637-59-2, 3-Phenylpropyl bromide 870-63-3, 1-Bromo-3-methylbut-2-ene 874-89-5, 4-Hydroxymethylbenzonitrile 874-98-6, 3-(Bromomethyl)-1-methoxyphenyl 938-09-0, 2-Chloroethyl phenyl sulfone 1117-71-1, Methyl 4-bromocrotonate 1129-28-8, Methyl 3-(bromomethyl)benzoate 1943-82-4. Phenethyl isocyanate 2144-37-8, Methyl 5-(chloromethyl)-2-furoate 2393-23-9, 4-Methoxybenzylamine 2417-72-3, Methyl 4-(bromomethyl)benzoate 2550-36-9. (Bromomethyl)cyclohexane 2620-50-0. Piperonylamine 2969-81-5. Ethyl 4-bromobutyrate 3113-72-2, 5-Methyl-2-nitrobenzoic acid 3173-56-6. Benzyl isocyanate 3277-89-2. Phenethylmagnesium bromide 3395-91-3. Methyl 3-bromopropanoate 3731-52-0, 3-(Aminomethyl)pyridine 3731-53-1, 4-Picolylamine 4070-48-8 4637-24-5 5071-96-5, 3-Methoxybenzylamine 5586-89-0 5794-88-7, 2-Amino-5-bromobenzoic acid 6232-11-7, Methyl 4-(aminomethyl)benzoate hydrochloride 6321-07-9. 4-Morpholin-4ylbutylamine 6482-24-2, 1-Bromo-2-methoxyethane 7005-47-2. 2-(Dimethylamino)-2-methylpropanol 7051-34-5, Cyclopropylmethyl bromide 7149-10-2, 4-Hydroxy-3-methoxybenzylamine hydrochloride 7398-42-7. Methyl 4-(bromomethyl)phenylacetate 10406-25-4 13734-41-3 17201-43-3, 4-(Bromomethyl)benzonitrile 18469-52-8, Methyl 4-aminomethyl benzoate 19059-68-8, 3-(Dimethylamino)-2.2-dimethylpropanol 22059-22-9. N-Hydroxyacetamidine 22600-30-2. Methyl 5-amino-2-furan carboxylate 25589-18-8, 3-Benzyl-6-methyl-1H-pyrimidine-2.4-dione 26146-77-0, (E)-Cinnamyl bromide 27757-85-3, 2-Thienylmethylamine 28188-41-2. 3-(Bromomethyl)benzonitrile 30260-66-3. Dimethylhydrazine 30280-44-5, 4-Chlorobenzyl isocyanate 32863-31-3, 5-Bromomethylbenzofurazan 39077-96-8 40724-47-8, 4-Bromomethylbenzenesulfonamide 41886-04-8, 3-Bromomethyl-1methylpiperidine 50541-93-0, 4-Amino-1-benzylpiperidine 55401-97-3. 2-(Bromomethyl)pyridine 56651-60-6, 4-Methoxybenzyl isocyanate 69966-55-8, 3-(Bromomethyl)pyridine 72235-53-1, 3,4-Difluorobenzylamine 72235-56-4, 3-Chloro-4-fluorobenzylamine 74733-27-0, Methyl 4-bromomethy1-2-methoxybenzoate 74733-28-1. Methyl 4-bromomethy1-2methyl benzoate 78358-86-8, 1-(2-Bromoethyl)pyrrole 78826-46-7. (tert-Butoxy)acetyl chloride 83171-39-5, 4-Methylthiobenzylamine 85070-57-1, Methyl 4-(bromomethyl)-2-fluorobenzoate 85147-14-4 88442-63-1, 1-(1-Naphthyl)ethyl isocyanate 89583-07-3, 4-(2-Bromoethyl)morpholine 93919-56-3. 4-Trifluoromethoxybenzylamine 99067-96-6, (4-(Dimethylamino)benzyl)isocyanate 102422-56-0, 3-Fluorobenzyl isocyanate 108052-76-2, tert-Butyl 4-bromomethylbenzoate 108499-32-7, Methyl 5-bromomethylthiophene-2-carboxylate 114772-38-2 114772-54-2, 2-(4-Bromomethylphenyl)benzonitrile 120788-70-7, Ethyl 1.3-dimethyl-2.4-dioxo-1.2.3.4-tetrahydropyrido[2.3-d]pyrimidine-6carboxylate 128674-45-3, 4-(3-Chloropropenyl)pyridine hydrochloride 138402-33-2 138895-24-6, 6-Amino-3-benzyl-1H-pyrimidine-2,4-dione 148900-69-0 154470-79-8, Methyl 1,3-dimethyl-2,4-dioxo-1,2,3.4tetrahydropyrido[3.4-d]pyrimidine-6-carboxylate 155965-45-0 220875-89-8, 5-(4-Chloromethylphenyl)-1-methyl-1H-tetrazole 221031-44-3, 2-Chloro-1-(4-diethylaminophenyl)ethan-1-one 302912-23-8. 4-Bromobenzyl isocyanate 304873-96-9, tert-Butyl (5-bromomethylpyridin-2-yl)carbamate 448965-87-5, tert-Butyl 1-(4-bromomethylphenyl)cyclopropanecarboxylate

449208-54-2. 1-Methyl-2.4-dioxo-1.2.3.4-tetrahydroquinazoline-6-carboxylic acid 449209-03-4. 3-((E)-3-Chloropropenyl)pyridine 4-((E)-3-Chloropropenyl)pyridine 449209-08-9. 3-(4-(Methanesulfonyl)benzyl)-1-methyl-2,4-dioxo-1,2,3,4-tetrahydroquinazoline-6-carboxylic acid 449209-35-2, 3-(4-Chloromethylphenyl)-5methyl[1,2,4]oxadiazole 449209-38-5, Methyl 2-chloro-4chloromethylbenzoate 449209-42-1. 5-(4-Chloromethylphenyl)-2-methyl-2Htetrazole 449209-56-7

RL: RCT (Reactant); RACT (Reactant or reagent)

(reactant; preparation of quinazolines as specific inhibitors of type-13 matrix metalloprotease)

RE.CNT 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD RF

- (1) Abou-Hadeed, K: PTERIDINES 1996, V7(4), P113 HCAPLUS
- (2) Anon; AMBINTER: EXPLORATORY LIBRARY 2002
- (3) Anon: CHEMSTAR PRODUCT LIST 2001
- (4) Anon: SCIENTIFIC EXCHANGE PRODUCT LIST 2001
- (5) Anon: SCREENING COLLECTION 2000
- (6) Bemis, G: WO 9964400 A 1999 HCAPLUS
- (7) Brittelli. D: WO 9743239 A 1997 HCAPLUS
- (8) Chen, J; JOURNAL OF THE AMERICAN CHEMICAL SOCIETY 2000, V122, P9648 HCAPLUS
- (9) Ciba Geigy Ag; DE 2441959 A 1975 HCAPLUS
- (10) Ghose, A; J MED CHEM 1984, V27(7), P901 HCAPLUS
- (11) Kim, Y; CHEMISTRY AND BIOLOGY OF PTERIDINES AND FOLATES 1997, PROCEEDINGS OF THE INTERNATIONAL SYMPOSIUM ON PTERIDINES AND FOLATES, 11TH 1997, P41
- (12) Lespagnol, A; BULL SOC PHARM LILLE 1977, V33(1), P67 HCAPLUS
- (13) Liverton, N; BIOORGANIC & MEDICINAL CHEMISTRY LETTERS 1998, V8(5), P483 **HCAPLUS**
- (14) Murata, S; CHEMISTRY AND BIOLOGY OF PTERIDINES AND FOLATES 1997. PROCEEDINGS OF THE INTERNATIONAL SYMPOSIUM ON PTERIDINES AND FOLATES, 11TH 1997. P17 HCAPLUS
- (15) Nesterov: SU 119879 A 1959 HCAPLUS
- (16) Ogawa, H: CHEM PHARM BULL 1988, V36(6), P2253 HCAPLUS
- (17) Reiter, L; BIOORGANIC & MEDICINAL CHEMISTRY LETTERS 1999, V9(2), P127 **HCAPLUS**
- (18) Sladowska, H; FARMACO, ED SCI 1986, V41(12), P954 HCAPLUS
- 449210-07-5P, 4-[[6-(4-Methoxybenzylcarbamoyl)-1-methyl-2,4-dioxo-1,4-dihydro-2H-pyrido[2,3-d]pyrimidin-3-yl]methyl]benzoic acid 449210-11-1P 449210-20-2P, Methyl 4-[[6-(4-Methoxybenzylcarbamoyl)-1-methyl-2,4-dioxo-1,4-dihydro-2H-pyrido[3,4d]pyrimidin-3-yl]methyl]benzoate 449210-24-6P. 4-[[6-(3-Methoxybenzylcarbamoyl)-1-methyl-2.4-dioxo-1.4-dihydro-2Hpyrido[3,4-d]pyrimidin-3-yl]methyl]benzoic acid 449210-27-9P 449210-47-3P, 4-[[6-(4-Methoxybenzylcarbamoyl)-1-methyl-2,4-dioxo-1,4-dihydro-2H-pyrido[3,4-d]pyrimidin-3-yl]methyl]benzoic acid RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES

(Uses) (MMP13 inhibitor; preparation of quinazolines as specific inhibitors of type-13 matrix metalloprotease)

449210-07-5 HCAPLUS

Benzoic acid, 4-[[1,4-dihydro-6-[[(4-methoxyphenyl)methyl]amino]carbonyl]-1-methyl-2,4-dioxopyrido[2,3-d]pyrimidin-3(2H)-yl]methyl]- (9CI) (CA INDEX NAME)

RN 449210-11-1 HCAPLUS

CN Pyrido[2,3-d]pyrimidine-6-carboxamide. 3-[(4-cyanophenyl)methyl]-1.2.3.4-tetrahydro-N-[(4-methoxyphenyl)methyl]-1-methyl-2,4-dioxo- (9CI) (CA INDEX NAME)

RN 449210-20-2 HCAPLUS

CN Benzoic acid, 4-[[1.4-dihydro-6-[[[(4-methoxyphenyl)methyl]amino]carbonyl]1-methyl-2.4-dioxopyrido[3.4-d]pyrimidin-3(2H)-yl]methyl]-, methyl ester
(9CI) (CA INDEX NAME)

RN 449210-24-6 HCAPLUS

CN Benzoic acid. 4-[[1.4-dihydro-6-[[[(3-methoxyphenyl)methyl]amino]carbonyl]1-methyl-2.4-dioxopyrido[3.4-d]pyrimidin-3(2H)-yl]methyl]- (9CI) (CA
INDEX NAME)

RN 449210-27-9 HCAPLUS

CN Pyrido[3,4-d]pyrimidine-6-carboxamide, 3-[(4-cyanophenyl)methyl]-1,2,3,4-tetrahydro-N-[(4-methoxyphenyl)methyl]-1-methyl-2,4-dioxo- (9CI) (CA INDEX NAME)

RN 449210-47-3 HCAPLUS

CN Benzoic acid. 4-[[1.4-dihydro-6-[[[(4-methoxyphenyl)methyl]amino]carbonyl]1-methyl-2,4-dioxopyrido[3,4-d]pyrimidin-3(2H)-yl]methyl]- (9CI) (CA
INDEX NAME)

CN Benzoic acid, 4-[[1,4-dihydro-6-[[[(4-methoxyphenyl)methyl]amino]carbonyl]1-methyl-2,4-dioxopyrido[2,3-d]pyrimidin-3(2H)-yl]methyl]-, methyl ester
(9CI) (CA INDEX NAME)

L26 ANSWER 4 OF 4 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 2002:637472 HCAPLUS

DN 137:201321

ED Entered STN: 23 Aug 2002

TI Preparation of substituted isophthalic acid derivatives, multicyclic pyrimidinediones and analogs thereof as matrix metalloproteinase inhibitors

IN Andrianjara, Charles: Ortwine, Daniel Fred; Pavlovsky, Alexander Gregory; Roark, William Howard

PA Warner-Lambert Company, USA

SO PCT Int. Appl., 173 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM . A61K

CC 28-16 (Heterocyclic Compounds (More Than One Hetero Atom)) Section cross-reference(s): 1, 63

FAN CNT 1

FAN.	CNI 1										
	PATENT NO.	KIN	KIND DATE		APPLICATION NO.				DATE		
PΙ	WO 2002064080		A2 20020822		WO 2002-IB447				20020213		
	WO 2002064080	A3	A3 20021212								
	W: AE, AG	, AL, AM,	AT, AU,	AZ, BA	BB. B	G. BR.	BY, BZ,	CA.	CH,	CN.	
	CO, CR	, CU, CZ.	DE, DK,	DM, DZ	EC, E	E, ES,	FI. GB.	GD.	GE,	GH,	
	GM, HR	, HU, ID,	IL, IN,	IS, JP	KE, K	G, KP,	KR, KZ,	LC.	LK.	LR,	
	LS, LT	. LU. LV.	MA, MD,	MG. MK.	MN, M	W, MX,	MZ, NO,	NZ,	OM,	PH,	
	PL, PT	, RO, RU.	SD. SE.	SG, SI	SK, S	L, TJ,	TM. TN.	TR.	Π,	TZ,	
	UA, UG	. US. UZ.	VN. YU.	ZA, ZM	, ZW, A	M, AZ,	BY, KG.	ΚZ,	MD.	RU.	
	TJ, TM										
	RW: GH, GM	, KE, LS,	MW. MZ.	SD, SL	SZ, T	Z, UG,	ZM, ZW,	ΑT,	BE,	CH,	
	CY, DE	, DK, ES,	FI. FR.	GB, GR	IE, I	T, LU,	MC, NL,	PΤ,	SE,	TR,	
	BF, BJ	, CF, CG,	CI. CM.	GA, GN	GQ, G	W. ML.	MR, NE,	SN,	TD,	TG	
	CA 2437643	A/	AA 20020822 CA 2002-2437643				543	20020213			
	US 2003078276	A1	A1 20030424 US 2002-75069					20020213			

```
EP 1361873
                        A2 20031119
                                           EP 2002-710275
                                                                 20020213
         R: AT. BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
                               20040309
     BR 2002007864
                                           BR 2002-7864
                                                                 20020213
     JP 2004529874
                                           JP 2002-563877
                               20040930
                                                                 20020213
                         T2
     US 2005004126
                                           US 2004-835619
                         A1
                               20050106
                                                                 20040429
PRAI US 2001-268821P
                         Ρ
                               20010214
     US 2002-75069
                         В3
                               20020213
     WO 2002-IB447
                         W
                               20020213
CLASS
 PATENT NO.
                CLASS PATENT FAMILY CLASSIFICATION CODES
                ....
 WO 2002064080 ICM
                       A61K
 JP 2004529874 FTERM 4C022/CA02; 4C036/AD05; 4C036/AD12; 4C036/AD19;
                       4C036/AD27; 4C036/AD30; 4C050/AA01; 4C050/AA07;
                       4C050/BB06; 4C050/CC08; 4C050/EE04; 4C050/FF03;
                       4C050/GG03; 4C050/HH02; 4C055/AA01; 4C055/BB01;
                       4C055/CA01; 4C055/DA06; 4C055/DA17; 4C055/DB04;
                       4C055/DB08: 4C055/EA01: 4C063/AA01: 4C063/AA03:
                       4C063/BB08; 4C063/BB09; 4C063/CC31; 4C063/CC81;
                       4C063/CC92: 4C063/DD12: 4C063/DD31: 4C063/EE01:
                       4C065/AA04; 4C065/BB11; 4C065/CC01; 4C065/DD03;
                       4C065/EE03; 4C065/HH08; 4C065/JJ01; 4C065/LL04;
                       4C065/PP18: 4C071/AA01: 4C071/BB01: 4C071/CC21:
                       4C071/EE13; 4C071/FF05; 4C071/GG02; 4C071/HH08;
                       4C071/HH28; 4C071/JJ01; 4C071/LL01; 4C072/AA01;
                       4C072/BB02; 4C072/CC02; 4C072/CC16; 4C072/EE12;
                       4C072/FF09: 4C072/GG07: 4C072/GG09: 4C072/HH02:
                       4C072/UU01: 4C086/AA01: 4C086/AA02: 4C086/AA03:
                       4C086/BA13; 4C086/BC17; 4C086/BC46; 4C086/BC87;
                       4C086/CB05; 4C086/CB09; 4C086/CB26; 4C086/GA04;
                       4C086/GA07; 4C086/GA08; 4C086/GA10: 4C086/MA01;
                       4C086/MA04; 4C086/NA14; 4C086/ZA02; 4C086/ZA36;
                       4C086/ZA45; 4C086/ZA59; 4C086/ZA67; 4C086/ZA89;
                       4C086/ZA96; 4C086/ZA97; 4C086/ZB11; 4C086/ZB15;
                       4C086/ZB26; 4H006/AA01; 4H006/AA03; 4H006/AB20;
                       4H006/AB22; 4H006/AB23; 4H006/AB25; 4H006/AB27;
                       4H006/AB28: 4H006/BJ50: 4H006/BM30: 4H006/BM71:
                       4H006/BM72; 4H006/BP30; 4H006/BR30; 4H006/BT32;
                       4H006/BU26: 4H006/BV72: 4H006/KC30
                ECLA
                       A61K031/00; C07D213/30D2; C07D213/40B; C07D239/96;
 US 2005004126
                       C07D285/14D: C07D285/24: C07D317/54: C07D317/58:
                       C07D401/06+239+211: C07D401/06+239+213:
                       C07D401/12+239+213; C07D405/12+317+213;
                       C07D405/12+317+239; C07D405/14+317+239+213;
                       C07D405/14+317+317+239; C07D409/06+333B+239;
                       C07D409/12+333B+239; C07D409/14+333B+239+213;
                       C07D409/14+333B+317+239; C07D471/04+239B+221B;
                       C07D487/04+235C+239C; C07D487/04+249C+239C;
                       C07D495/04+333B+239B; C07D513/04+277C+239C
GΙ
```

- Title compds.. I [R1 and R2 together may form a substituted aromatic ring or a heterocyclic ring; or R2 and R3 together may form substituted heterocycle; or R1, R3, or R4 = alkyl, arylalkyl, etc.; X = C, S; Y = O, N with provision when Y = N it forms a 5-membered heterocycle with R3] and II [R5. R6 = arylalkylamine, heterocyclylalkoxy, etc.; R7 = H, MeO, NO2, etc.], are prepared and disclosed as matrix metalloproteinase (MMP) inhibitors. Thus, III was prepared in five steps via cyclocondensation of diethylmalonate and benzylurea with subsequent chlorination, substitution with hydrosulfide hydrate to form an in situ intermediate that was reacted with bromoacetaldehyde dimethylacetal, followed by acid catalyzed cyclization and substitution with benzylchloroformate. III was demonstrated to inhibit MMP13 with an IC50 value (in .mu.M) of 0.0230. I and II bind allosterically to the catalytic domain of MMP-13 and comprise a hydrophobic group, first and second hydrogen bond acceptors and at least one, and preferably both, of a third hydrogen bond acceptor and a second hydrophobic group. Cartesian coordinates for centroids of the above features are defined in the specification. When the ligand binds to MMP-13, the first, second and third (when present) hydrogen bond acceptors bond resp. with Thr245, Thr247 and Met 253, the first hydrophobic group locates within the S1' channel of MMP-13 and the second hydrophobic group (when present) is relatively open to solvent. The compds. specifically inhibit the matrix metalloproteinase-13 enzyme and thus are useful for treating diseases resulting from tissue breakdown, such as heart disease. multiple sclerosis, arthritis, atherosclerosis, and osteoporosis.
- ST pyrimidinedione prepn matrix metalloproteinase inhibitor; isophthalic carboxylate prepn matrix metalloproteinase inhibitor; metalloproteinase inhibitor pyrimidinedione antiinflammatory
- IT Antiarteriosclerotics

(antiatherosclerotics: preparation and pharmaceutical activity of substituted isophthalic acid derivs.. multicyclic pyrimidinediones and analogs thereof as matrix metalloproteinase inhibitors)

IT Lung, disease

(chronic obstructive; preparation and pharmaceutical activity of substituted isophthalic acid derivs., multicyclic pyrimidinediones and analogs thereof as matrix metalloproteinase inhibitors)

IT Heart, disease

(failure: preparation and pharmaceutical activity of substituted isophthalic acid derivs., multicyclic pyrimidinediones and analogs thereof as matrix metalloproteinase inhibitors)

IT Intestine, disease

(inflammatory; preparation and pharmaceutical activity of substituted isophthalic acid derivs.. multicyclic pyrimidinediones and analogs thereof as matrix metalloproteinase inhibitors)

IT Combinatorial library

(isopthalic acid derivs.; combinatorial preparation and pharmaceutical activity of substituted isophthalic acid derivs. as matrix metalloproteinase inhibitors)

```
Eye, disease
        (macula, senile degeneration; preparation and pharmaceutical activity of
       substituted isophthalic acid derivs., multicyclic pyrimidinediones and
       analogs thereof as matrix metalloproteinase inhibitors)
IT Anti-inflammatory agents
    Antiarthritics
    Antiasthmatics
    Antirheumatic agents
    Antitumor agents
    Arthritis
    Asthma
    Atherosclerosis
    Cardiovascular agents
    Human
    Multiple sclerosis
    Neoplasm
    Osteoarthritis
    Osteoporosis
    Periodontium, disease
    Psoriasis
    Rheumatoid arthritis
        (preparation and pharmaceutical activity of substituted isophthalic acid
       derivs., multicyclic pyrimidinediones and analogs thereof as matrix
       metalloproteinase inhibitors)
IT
    Multiple sclerosis
    Osteoporosis
       (therapeutic agents; preparation and pharmaceutical activity of substituted
       isophthalic acid derivs., multicyclic pyrimidinediones and analogs
       thereof as matrix metalloproteinase inhibitors)
                  449790-84-5P 449790-90-3P 449791-35-9P
    449790-74-3P
    RL: CPN (Combinatorial preparation): PAC (Pharmacological activity): THU
    (Therapeutic use): BIOL (Biological study); CMBI (Combinatorial study):
    PREP (Preparation): USES (Uses)
       (combinatorial preparation and pharmaceutical activity of substituted
       isophthalic acid derivs. as matrix metalloproteinase inhibitors)
    1459-93-4P. Dimethyl isophthalate 4315-09-7P, 4-Nitroisophthalic acid
    5759-76-2P 13756-42-8P, 4-Methylbenzoic acid tert-butyl ester
    63746-12-3P, Dimethyl 4-aminoisophthalate 69048-70-0P, Dimethyl
    4-nitroisophthalate 91360-95-1P 108052-76-2P, tert-Butyl-4-
    (bromomethyl)benzoate 175143-75-6P 177913-48-3P. Dimethyl
    4-amino-1-hydroxycyclohexa-3,5-diene-1,3-dicarboxylate 209604-61-5P
    221540-53-0P
                   342644-48-8P
                                  448964-68-9P
                                                 448964-69-0P
                                                                448964-70-3P
    449207-91-4P
                   449207-94-7P
                                  449207-95-8P
                                                 449208-21-3P
                                                                449208-24-6P
    449208-33-7P
                   449208-34-8P
                                  449208-35-9P
                                                 449208-43-9P
                                                                449208-44-0P
                                                                449210-06-4P
    449208-45-1P
                   449208-51-9P
                                  449208-53-1P
                                                 449210-05-3P
    449210-08-6P
                   449210-09-7P 449210-10-0P 449210-14-4P.
    1-Benzyl-2,6-dioxo-1,2,3,6-tetrahydropyrimidine-4-carboxaldehyde
                                 449210-17-7P 449210-18-8P
    449210-15-5P
                   449210-16-6P
                                                                449210-19-9P
    449210-21-3P
                   449210-22-4P
                                  449211-37-4P
                                                 449211-38-5P
                                                                449755-90-2P
    449755-91-3P
                   449755-92-4P
                                  449755-95-7P
                                                 449755-96-8P
                                                                449798-65-6P
    449798-67-8P, 6-Benzylthiazolo[3,2-c]pyrimidine-5.7-dione
                                                                449798-69-0P
    449798-70-3P
                   449798-72-5P
                                  449798-74-7P
                                                 449799-51-3P
                                                                449799-52-4P
    449799-63-7P
                   449799-64-8P
                                  451471-59-3P
                                                 451471-60-6P
                                                                451471-61-7P
    451471-62-8P
                   451471-63-9P
                                  451471-64-0P
                                                 451471-65-1P
                                                                451471-66-2P
    451471-67-3P
                   451471-68-4P
                                  451471-69-5P
                                                 451471-70-8P
                                                                451471-71-9P
    451471-72-0P
                   451471-73-1P
                                  451471-74-2P
                                                 451471-75-3P
    RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
    (Reactant or reagent)
       (intermediate: preparation and pharmaceutical activity of substituted
       isophthalic acid derivs., multicyclic pyrimidinediones and analogs
       thereof as matrix metalloproteinase inhibitors)
   9001-12-1. Matrix metalloproteinase-1 79955-99-0, Matrix
    metalloproteinase-3 141256-52-2, Matrix metalloproteinase-7
    146480-35-5, Matrix metalloproteinase-2 146480-36-6, Matrix
```

```
metalloproteinase-9 161384-17-4. Matrix metalloproteinase-14
 175449-82-8. Collagenase 3
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
     (preparation and pharmaceutical activity of substituted isophthalic acid
     derivs.. multicyclic pyrimidinediones and analogs thereof as matrix
     metalloproteinase inhibitors)
149277-46-3, GenBank A0000434
 RL: BSU (Biological study, unclassified); PRP (Properties); BIOL
 (Biological study)
     (preparation and pharmaceutical activity of substituted isophthalic acid
     derivs., multicyclic pyrimidinediones and analogs thereof as matrix
     metalloproteinase inhibitors)
 100-46-9. Benzyl amine, reactions 104-86-9, 4-Chlorobenzyl amine
 2393-23-9, 4-Methoxybenzylamine 2620-50-0, Piperonyl amine RL: CRT (Combinatorial reactant); RCT (Reactant); CMBI (Combinatorial
 study); RACT (Reactant or reagent)
     (preparation and pharmaceutical activity of substituted isophthalic acid
     derivs.. multicyclic pyrimidinediones and analogs thereof as matrix
     metalloproteinase inhibitors)
 449792-10-3P
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
 (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
 (Uses)
     (preparation and pharmaceutical activity of substituted isophthalic acid
     derivs.. multicyclic pyrimidinediones and analogs thereof as matrix
    metalloproteinase inhibitors)
 96-33-3, Methyl acrylate 99-63-8, 1.3-Benzenedicarbonyl dichloride
 100-11-8, 4-Nitrobenzylbromide 100-51-6, Benzyl alcohol, reactions
 105-53-3. Diethylmalonate 108-90-7. Chlorobenzene. reactions 140-88-5. Ethyl acrylate 459-46-1. 4-Fluorobenzyl bromide 495-76-1. Piperonyl alcohol 501-53-1. Benzylchloroformate 538-32-9. Benzylurea 586-95-8.
 4-Pyridinemethanol '609-08-5, Diethylmethyl malonate 623-51-8.
 Mercapto-acetic acid, ethyl ester 874-60-2, 4-Methylbenzoyl chloride
 1189-71-5, N-Chlorosulfonyl isocyanate 2206-43-1, 4-Methoxy-1,3-
 benzenedicarboxylic acid 2417-72-3. Methyl-4-(bromomethyl)benzoate
 3113-72-2. 5-Methyl-2-nitrobenzoic acid 3173-56-6. Benzylisocyanate
 3731-53-1, Pyridin-4-ylmethylamine 4392-24-9, Cinnamyl bromide
 4637-24-5 5326-47-6, 2-Amino-5-iodobenzoic acid 6232-11-7, Methyl 4-(aminomethyl)benzoate, hydrochloride 6959-47-3, Picolyl chloride,
 hydrochloride 7149-10-2, 4-Hydroxy-3-methoxybenzylamine, hydrochloride
 7252-83-7. Bromoacetaldehyde dimethylacetal 10147-11-2.
 3-Phenyl-1-propyne 13235-60-4 13540-76-6, 3-(4-Methoxyphenyl)prop-1-
 yne 17201-43-3, 4-(Bromomethyl)benzonitrile 18358-63-9.
 Methyl-4-methylaminobenzoate 18469-52-8, Methyl 4-(aminomethyl)benzoate
 22600-30-2, Methyl-5-amino-2-furoate 25589-18-8, 3-Benzyl-6-methyl-1H-
 pyrimidine-2.4-dione 27757-85-3. 2-Thiophene methylamine 30280-44-5.
 4-Chlorobenzyl isocyanate 40517-43-9, 4-Methylsulfonylbenzyl chloride
 54751-01-8, 4-Bromomethylpyridine 56651-60-6, 4-Methoxybenzyl isocyanate
 138895-24-6, 6-Amino-3-benzyl-1H-pyrimidine-2,4-dione 183741-86-8
               305805-20-3 449208-54-2 449211-43-2 449798-87-2
 305804-90-4
 449799-49-9
 RL: RCT (Reactant): RACT (Reactant or reagent)
     (preparation and pharmaceutical activity of substituted isophthalic acid
     derivs., multicyclic pyrimidinediones and analogs thereof as matrix
    metalloproteinase inhibitors)
449790-79-8P
 RL: CPN (Combinatorial preparation); PAC (Pharmacological activity); SPN
 (Synthetic preparation): THU (Therapeutic use): BIOL (Biological study):
 CMBI (Combinatorial study); PREP (Preparation); USES (Uses)
     (target compound; combinatorial preparation and pharmaceutical activity of
     substituted isophthalic acid derivs. as matrix metalloproteinase
     inhibitors)
                 449208-01-9P
                                 449208-02-0P
                                                 449208-37-1P
                                                                 449208-39-3P
 448964-75-8P
```

449208-42-8P

449208-50-8P

449208-57-5P

449211-17-0P

```
preparation); THU (Therapeutic use); BIOL (Biological study); PREP
(Preparation); RACT (Reactant or reagent); USES (Uses)
   (target compound: preparation and pharmaceutical activity of substituted
   isophthalic acid derivs., multicyclic pyrimidinediones and analogs
   thereof as matrix metalloproteinase inhibitors)
                                                             167993-08-0P
16034-14-3P
              143569-91-9P
                              151107-61-8P
                                              152699-63-3P
                                               448964-82-7P
                                                              448964-84-9P
               383163-58-4P
                               448964-76-9P
349396-68-5P
                                                              448964-98-5P
448964-85-0P
               448964-86-1P
                               448964-90-7P
                                               448964-94-1P
448964-99-6P
               448965-31-9P
                               448965-33-1P
                                               448965-35-3P
                                                              448965-36-4P
448965-38-6P
               448965-39-7P
                               448965-41-1P
                                               448965-42-2P
                                                              448965-43-3P
448965-44-4P
               448965-46-6P
                               448965-47-7P
                                               448965-48-8P
                                                              448965-49-9P
448965-50-2P
               448965-51-3P
                               448965-57-9P
                                               448965-58-0P
                                                              448965-59-1P
448965-60-4P
               448965-64-8P
                               448965-66-0P
                                               448965-67-1P
                                                              448965-69-3P
                                               448965-73-9P
448965-70-6P
               448965-71-7P
                               448965-72-8P
                                                              448965-74-0P
                               448965-77-3P
                                               448965-78-4P
                                                              448965-79-5P
448965-75-1P
               448965-76-2P
448965-80-8P
               448965-82-0P
                               448965-89-7P
                                               448965-91-1P
                                                              448965-93-3P
                               448965-98-8P
                                               448965-99-9P
                                                              448966-00-5P
448965-96-6P
               448965-97-7P
448966-01-6P
               448966-02-7P
                               448966-03-8P
                                               448966-04-9P
                                                              448966-05-0P
                                               448966-10-7P
               448966-07-2P
                               448966-09-4P
                                                              448966-11-8P
448966-06-1P
448966-12-9P
               448966-13-0P
                               448966-14-1P
                                               448966-15-2P
                                                              448966-16-3P
448966-17-4P
               448966-19-6P
                               448966-21-0P
                                               448966-22-1P
                                                              448966-23-2P
                                                              448966-28-7P
                                               448966-27-6P
448966-24-3P
               448966-25-4P
                               448966-26-5P
                               448966-31-2P
                                               448966-32-3P
                                                              448966-33-4P
               448966-30-1P
448966-29-8P
448966-34-5P
                                               448966-42-5P
               448966-35-6P
                               448966-36-7P
                                                              448966-45-8P
448966-50-5P
               448966-52-7P
                               448966-53-8P
                                               448966-57-2P
                                                              448966-65-2P
                               448966-72-1P
                                               448966-75-4P
                                                              448966-77-6P
448966-68-5P
               448966-71-0P
                                               448966-87-8P
                                                              448966-88-9P
448966-78-7P
               448966-85-6P
                               448966-86-7P
448966-92-5P
               448966-94-7P
                               448966-95-8P
                                               448966-96-9P
                                                              448966-97-0P
               448967-05-3P
                               448967-06-4P
                                               448967-07-5P
                                                              448967-08-6P
448967-02-0P
                                                              448967-14-4P
               448967-10-0P
                               448967-12-2P
                                               448967-13-3P
448967-09-7P
448967-16-6P
               448967-19-9P
                               448967-20-2P
                                               448967-21-3P
                                                              448967-23-5P
448967-24-6P
               448967-25-7P
                               448967-26-8P
                                               448967-27-9P
                                                              448967-28-0P
448967-29-1P
               448967-30-4P
                               448967-31-5P
                                               448967-34-8P
                                                              448967-35-9P
                                               448967-44-0P
448967-38-2P
               448967-39-3P
                               448967-41-7P
                                                              448967-45-1P
448967-47-3P
               448967-48-4P
                               448967-49-5P
                                               448967-50-8P
                                                              448967-52-0P
448967-53-1P
               448967-54-2P
                               448967-56-4P
                                               448967-57-5P
                                                              448967-59-7P
448967-60-0P
               448967-61-1P
                               448967-63-3P
                                               448967-64-4P
                                                              448967-66-6P
                               448967-72-4P
                                                              448967-74-6P
                                               448967-73-5P
               448967-71-3P
448967-69-9P
448967-76-8P
               448967-80-4P
                               448967-81-5P
                                               448967-82-6P
                                                              448967-87-1P
448967-88-2P
               448967-92-8P
                               448967-93-9P
                                               448967-94-0P
                                                              448967-96-2P
448967-97-3P
               448967-98-4P
                               448967-99-5P
                                               448968-00-1P
                                                              448968-03-4P
                                               448968-19-2P
                                                              448968-23-8P
448968-11-4P
               448968-12-5P
                               448968-16-9P
448968-24-9P
               448968-27-2P
                               448968-28-3P
                                               448968-30-7P
                                                              448968-34-1P
                                               448968-43-2P
                                                              448968-44-3P
448968-35-2P
               448968-40-9P
                               448968-41-0P
448968-45-4P
               448968-49-8P
                               448968-51-2P
                                               448968-53-4P
                                                              448968-54-5P
448968-55-6P
               448968-68-1P
                               448968-69-2P
                                               448970-24-9P
                                                              449208-03-1P
449208-04-2P
               449208-06-4P
                               449208-07-5P
                                               449208-08-6P
                                                              449208-09-7P
               449208-11-1P
                               449208-12-2P
                                               449208-13-3P
                                                              449208-14-4P
449208-10-0P
                               449208-20-2P
                                               449208-22-4P
                                                              449208-23-5P
449208-15-5P
               449208-16-6P
               449208-32-6P
                               449208-36-0P
                                               449208-38-2P
                                                              449208-40-6P
449208-26-8P
449208-41-7P
               449208-46-2P
                               449208-47-3P
                                               449208-48-4P
                                                              449208-49-5P
449208-52-0P
               449208-55-3P
                               449208-58-6P
                                              449208-59-7P
                                                              449208-60-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
(Uses)
   (target compound; preparation and pharmaceutical activity of substituted
   isophthalic acid derivs.. multicyclic pyrimidinediones and analogs
   thereof as matrix metalloproteinase inhibitors)
449208-61-1P
               449208-62-2P
                               449208-63-3P
                                               449208-64-4P
                                                              449208-65-5P
                                                              449208-72-4P
449208-66-6P
               449208-69-9P
                               449208-70-2P
                                               449208-71-3P
                               449208-75-7P
                                               449208-76-8P
                                                              449208-77-9P
449208-73-5P
               449208-74-6P
               449208-79-1P
                                                              449208-82-6P
449208-78-0P
                               449208-80-4P
                                               449208-81-5P
449208-83-7P
               449208-84-8P
                               449208-85-9P
                                               449208-87-1P
                                                              449208-88-2P
```

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic

Truong 10/075954

449208-93-9P

449208-98-4P

449209-07-8P

449209-17-0P

449209-22-7P

449209-27-2P

449209-32-9P

449208-92-8P

449208-97-3P

449209-06-7P

449209-16-9P

449209-21-6P

449209-26-1P

449209-31-8P

```
449209-37-4P
                              449209-36-3P
                                                             449209-39-6P
449209-33-0P
               449209-34-1P
                              449209-43-2P
                                              449209-44-3P
                                                             449209-45-4P
449209-40-9P
               449209-41-0P
                              449209-48-7P
                                              449209-49-8P
                                                             449209-52-3P
449209-46-5P
               449209-47-6P
449209-53-4P
               449209-54-5P
                              449209-59-0P
                                              449209-60-3P
                                                             449209-61-4P
                              449209-65-8P
                                              449209-66-9P
                                                             449209-67-0P
               449209-64-7P
449209-63-6P
                              449209-70-5P
                                              449209-71-6P
                                                             449209-72-7P
449209-68-1P
               449209-69-2P
449209-75-0P
               449209-77-2P
                              449209-79-4P
                                              449209-81-8P
                                                             449209-82-9P
449209-83-0P
               449209-84-1P
                              449209-86-3P
                                              449209-89-6P
                                                             449209-90-9P
                              449209-97-6P
                                              449209-98-7P
                                                             449209-99-8P
449209-91-0P
               449209-94-3P
                              449210-03-1P 449210-07-5P
449210-00-8P
               449210-01-9P
449210-11-1P
               449210-12-2P
                              449210-13-3P 449210-20-2P
449210-24-6P 449210-27-9P
                            449210-28-0P
                                            449210-29-1P
                                                             449210-34-8P
449210-30-4P
               449210-31-5P
                              449210-32-6P
                                              449210-33-7P
               449210-37-1P
                              449210-38-2P
                                              449210-39-3P
                                                             449210-40-6P
449210-36-0P
449210-41-7P
               449210-42-8P
                              449210-45-1P 449210-47-3P
449210-49-5P
               449210-51-9P
                              449210-52-0P
                                              449210-53-1P
                                                             449210-54-2P
                              449210-57-5P
                                                             449210-62-2P
               449210-56-4P
                                              449210-61-1P
449210-55-3P
               449210-67-7P
                              449210-68-8P
                                              449210-72-4P
                                                             449210-74-6P
449210-66-6P
                              449210-78-0P
                                              449210-79-1P
                                                             449210-81-5P
449210-75-7P
               449210-76-8P
449210-82-6P
               449210-84-8P
                              449210-85-9P
                                              449210-87-1P
                                                             449210-88-2P
                                                             449210-97-3P
449210-89-3P
               449210-90-6P
                              449210-95-1P
                                              449210-96-2P
               449211-03-4P
                              449211-04-5P
                                              449211-05-6P
                                                             449211-06-7P
449211-02-3P
                              449211-09-0P
                                              449211-10-3P
                                                             449211-11-4P
449211-07-8P
               449211-08-9P
                                              449211-16-9P
449211-13-6P
               449211-14-7P
                              449211-15-8P
                                                             449211-18-1P
                              449211-21-6P
                                              449211-22-7P
                                                             449211-24-9P
449211-19-2P
               449211-20-5P
               449211-27-2P
                              449211-28-3P
                                              449211-29-4P
                                                             449211-30-7P
449211-25-0P
               449211-32-9P
                              449211-33-0P
                                              449211-34-1P
                                                             449211-35-2P
449211-31-8P
                              449754-50-1P
                                              449754-51-2P
                                                             449754-53-4P
449211-36-3P
               449754-49-8P
               449754-61-4P
                              449754-62-5P
                                              449754-64-7P
                                                             449754-65-8P
449754-59-0P
449754-66-9P
               449754-67-0P
                              449754-69-2P
                                              449754-70-5P
                                                             449754-72-7P
449754-73-8P
               449754-74-9P
                              449754-75-0P
                                              449754-76-1P
                                                             449754-77-2P
                                              449754-82-9P
                                                             449754-83-0P
449754-78-3P
               449754-79-4P
                              449754-80-7P
449754-84-1P
               449754-85-2P
                              449754-86-3P
                                              449754-87-4P
                                                             449754-88-5P
449754-89-6P
               449754-97-6P
                              449754-99-8P
                                              449790-17-4P
                                                             449790-22-1P
449790-25-4P
               449790-28-7P
                              449790-33-4P
                                              449790-36-7P
                                                             449790-39-0P
                                              449790-57-2P
                              449790-52-7P
               449790-45-8P
449790-42-5P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
(Uses)
   (target compound: preparation and pharmaceutical activity of substituted
   isophthalic acid derivs., multicyclic pyrimidinediones and analogs
   thereof as matrix metalloproteinase inhibitors)
                                                             449790-95-8P
449790-60-7P
               449790-66-3P
                              449790-70-9P
                                              449790-87-8P
449790-98-1P
               449791-01-9P
                                              449791-09-7P
                                                             449791-12-2P
                              449791-04-2P
449791-15-5P
               449791-18-8P
                              449791-20-2P
                                              449791-28-0P
                                                             449791-31-5P
449791-41-7P
               449791-44-0P
                              449791-47-3P
                                              449791-50-8P
                                                             449791-53-1P
                                              449791-65-5P
                              449791-62-2P
                                                             449791-68-8P
449791-56-4P
               449791-59-7P
               449791-74-6P
                              449791-77-9P
                                              449791-81-5P
                                                             449791-84-8P
449791-71-3P
449791-90-6P
               449791-93-9P
                              449791-96-2P
                                              449791-99-5P
                                                             449792-02-3P
449792-04-5P
               449792-07-8P
                              449792-13-6P
                                              449798-64-5P
                                                             449798-68-9P
                                                             449798-82-7P
                              449798-80-5P
                                              449798-81-6P
449798-71-4P
               449798-75-8P
449798-86-1P
               449798-88-3P
                              449798-90-7P
                                              449798-91-8P
                                                             449798-94-1P
449798-95-2P
               449798-97-4P
                              449799-02-4P
                                              449799-05-7P
                                                             449799-06-8P
                                                             449799-34-2P
449799-14-8P
               449799-16-0P
                              449799-19-3P
                                              449799-27-3P
449799-36-4P
               449799-37-5P
                              449799-38-6P
                                              449799-40-0P
                                                             449799-42-2P
                                              449799-50-2P
                                                              449799-53-5P
449799-43-3P
               449799-44-4P
                               449799-45-5P
                                                             449799-62-6P
449799-55-7P
               449799-58-0P
                              449799-59-1P
                                              449799-60-4P
```

449208-91-7P

449208-96-2P

449209-01-2P

449209-14-7P

449209-20-5P

449209-25-0P

449209-30-7P

449208-90-6P

449208-95-1P

449209-00-1P

449209-13-6P 449209-19-2P

449209-24-9P

449209-29-4P

449208-89-3P

449208-94-0P

449208-99-5P

449209-09-0P

449209-18-1P

449209-23-8P

449209-28-3P

IT

449799-71-7P 449799-70-6P 449799-65-9P 449799-66-0P 449799-67-1P 449799-72-8P 449799-73-9P 449799-74-0P 449799-76-2P 449799-77-3P 449799-78-4P 449799-79-5P 449799-80-8P 449799-81-9P 449799-84-2P 449799-90-0P 449799-85-3P 449799-86-4P 449799-87-5P 449799-89-7P 449799-97-7P 449799-98-8P 449800-01-5P 449799-93-3P 449799-96-6P 449800-03-7P 449800-04-8P 449800-05-9P 449800-07-1P 449800-08-2P 449800-13-9P 449800-15-1P 449800-19-5P 449800-09-3P 449800-12-8P 451471-31-1P 451471-32-2P 451471-33-3P 451471-34-4P 451471-35-5P 451471-36-6P 451471-37-7P 451471-38-8P 451471-39-9P. Thieno[2,3-d]pyrimidine-6-carboxylic acid benzyl ester 451471-40-2P 451471-42-4P 451471-43-5P 451471-44-6P 451471-45-7P 451471-41-3P 451471-51-5P 451471-47-9P 451471-48-0P 451471-49-1P 451471-50-4P 451471-54-8P 451471-55-9P 451471-56-0P 451471-52-6P 451471-53-7P 451471-57-1P 451471-58-2P 451473-18-0P RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(target compound: preparation and pharmaceutical activity of substituted isophthalic acid derivs., multicyclic pyrimidinediones and analogs thereof as matrix metalloproteinase inhibitors)

IT 452379-12-3

RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)

(unclaimed protein sequence; preparation and pharmaceutical activity of substituted isophthalic acid derivs., multicyclic pyrimidinediones and analogs thereof as matrix metalloproteinase inhibitors)

IT 449210-10-0P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(intermediate: preparation and pharmaceutical activity of substituted isophthalic acid derivs.. multicyclic pyrimidinediones and analogs thereof as matrix metalloproteinase inhibitors)

RN 449210-10-0 HCAPLUS

SN Benzoic acid, 4-[[1.4-dihydro-6-[[[(4-methoxyphenyl)methyl]amino]carbonyl]1-methyl-2.4-dioxopyrido[2.3-d]pyrimidin-3(2H)-yl]methyl]-, methyl ester
(9CI) (CA INDEX NAME)

TT 449210-07-5P 449210-11-1P 449210-20-2P 449210-24-6P 449210-27-9P 449210-47-3P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(target compound; preparation and pharmaceutical activity of substituted isophthalic acid derivs.. multicyclic pyrimidinediones and analogs thereof as matrix metalloproteinase inhibitors)

N 449210-07-5 HCAPLUS

CN Benzoic acid. 4-[[1.4-dihydro-6-[[[(4-methoxyphenyl)methyl]amino]carbonyl]1-methyl-2.4-dioxopyrido[2.3-d]pyrimidin-3(2H)-yl]methyl]- (9CI) (CA
INDEX NAME)

RN 449210-11-1 HCAPLUS

CN Pyrido[2,3-d]pyrimidine-6-carboxamide. 3-[(4-cyanophenyl)methyl]-1,2,3,4-tetrahydro-N-[(4-methoxyphenyl)methyl]-1-methyl-2,4-dioxo- (9CI) (CA INDEX NAME)

RN 449210-20-2 HCAPLUS

CN Benzoic acid. 4-[[1.4-dihydro-6-[[[(4-methoxyphenyl)methyl]amino]carbonyl]1-methyl-2,4-dioxopyrido[3,4-d]pyrimidin-3(2H)-yl]methyl]-. methyl ester
(9CI) (CA INDEX NAME)

RN 449210-24-6 HCAPLUS

CN Benzoic acid, 4-[[1,4-dihydro-6-[[[(3-methoxyphenyl)methyl]amino]carbonyl]1-methyl-2,4-dioxopyrido[3,4-d]pyrimidin-3(2H)-yl]methyl]- (9CI) (CA
INDEX NAME)

RN 449210-27-9 HCAPLUS

CN Pyrido[3,4-d]pyrimidine-6-carboxamide, 3-[(4-cyanophenyl)methyl]-1.2,3,4-tetrahydro-N-[(4-methoxyphenyl)methyl]-1-methyl-2,4-dioxo- (9CI) (CA INDEX NAME)

RN 449210-47-3 HCAPLUS

CN Benzoic acid. 4-[[1.4-dihydro-6-[[(4-methoxyphenyl)methyl]amino]carbonyl]1-methyl-2,4-dioxopyrido[3,4-d]pyrimidin-3(2H)-yl]methyl]- (9CI) (CA
INDEX NAME)

=> b home

FILE 'HOME' ENTERED AT 13:44:45 ON 07 FEB 2005

=>